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A Study of Intestinal Flatulence*

By John L. Kantor, M.D., and Jerome A. Marks, M.D., *New York*

I. PHYSIOLOGY OF GAS IN THE INTESTINE

NORMALLY gas is present in the intestine in small amounts, insufficient to cause annoyance. It is readily passed, chiefly with the bowel movements, and is for the most part, odorless. The origin of this gas is two-fold, from the atmospheric air, and from food-stuffs.

Atmospheric air is swallowed during eating, and especially while drinking. By far the greater part of the ingested air is quickly belched. What little is left in the stomach assumes significance because it is composed of 80% nitrogen which is practically unabsorbable by the body and 20% oxygen which is absorbed in part only. This residue, accordingly, is forced to make the transit of the entire digestive tract, and appears almost quantitatively in the flatus.

Enormous quantities of gas must be produced during the intestinal phase of digestion, the exact amount and composition depending upon the diet. Inasmuch as most of this gas is readily absorbed in the blood stream, to be fixed there or exhaled through the expired air, the healthy individual remains entirely unconscious of this phase of digestion. By far the greatest part of the gas produced by food digestion is carbon dioxide. This has the following sources: (1) In the upper small intestine, from a mixture of the acid gastric contents with the carbonates present in the alkaline biliary and pancreatic secretions. The amount thus manufactured has been estimated by v. Bunge[7] at six liters daily. (2) In the lower small intestine from the *possible* bacterial decomposition of sugars. It is to be recalled that sugars and starches are normally broken down by enzymic action to monosaccharids which are readily absorbed as such. It does not seem likely that, in health, much monosaccharid would be available for decomposition to CO_2 by bacterial action. At any rate no figures are available in the literature. (3) In the ceco-colon from the bacterial decomposition of cellulose, there being, in man, no enzyme capable of attacking this substance. Cellulose produces CO_2 and fatty acids, which in turn, liberate more CO_2 when neutralized by the alkaline carbonates secreted in the proximal colon.

Other gases, normally present in small amounts, are marsh gas (CH_4) and hydrogen, from cellulose, and occasionally traces of indol, skatol, hy-

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drogen sulfid, and ammonia, from the putrefaction of proteins. The last four gases are odoriferous; CH_4 and H_2 are inflammable. Carbon dioxid is by far the most readily absorbable gas, nitrogen the least; the other gases range as follows in order of their absorbability: H_2S, O_2, H_2, CH_4. For details see Fig. 1.

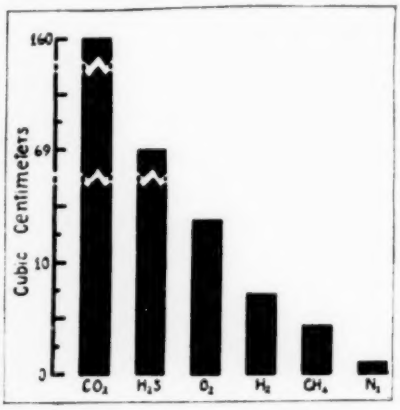

FIG. 1. Relative rates of absorption of various gases introduced into the intestine (after McIver).

Gas absorption has been shown to follow the physical laws of diffusion (Dunn and Thompson[8], McIver[25]). It has been definitely demonstrated that the walls of the intestine are permeable to gases and that an active interchange takes place, tending to keep the gases on the two sides of the mucosa in equilibrium. As Alvarez[1] has pointed out, the chief feature of interest in this connection is that when N_2 is diffused into the bowel, it is not reabsorbed, not only because of its low diffusion constant but also because the blood and tissues are already saturated with this gas.

Intestinal flatus is therefore to be regarded as a resultant, at any given moment, of air admixture, gas production from food digestion, gas absorption from the intestine and possible gas diffusion into the intestine, the last named factor being probably unimportant in health. In flatus, as might be expected, it is the unabsorbable gases that predominate, as may be seen in the following analysis by Fries[14]:

CO_2	10.3	volumes per cent.
O_2	0.7	volumes per cent.
CH_4	29.6	volumes per cent.
N	29.4	volumes per cent.

Inasmuch as no nitrogen is produced during digestion, all of this gas is assumed to result either from the air originally swallowed, or from gas secreted from the blood in the process of equilibration.

The amount of gas passed per rectum is estimated at I liter daily (Fries). This is to be contrasted with the much greater amount absorbed. Tacke[35] working with rabbits, found that ten to twenty times as much intestinal gas escapes by the lungs as by direct expulsion from the lower bowel. The figures for man are unavailable.

II. PATHOLOGY OF GAS IN THE INTESTINE (FLATULENCE, METEORISM, ETC.)

Incidence—Intestinal flatulence appears to be one of the more common symptoms encountered in practice. It occurred in 500 (33%) of a series of 1496 private patients complaining of various disorders of digestion. Flatulence ranked third among the ten most frequent complaints in this group (see table I).

TABLE I.

Incidence of the More Common Complaints of Dyspeptics
(Based on 2,500 histories)

SYMPTOM OR CONDITION	INCIDENCE (PER CENT.)
1. Constipation	46.5
2. Abdominal Pain	46.2
3. Flatulence	33.4
4. Belching	33.1
5. Headaches	22.8
6. Vomiting	19.7
7. Epigastric Distress	13.3
8. Heartburn	10.8
9. Weight Loss	7.4
10. Diarrhea	7.1

TABLE II.

Relation of Flatulence to Some Common Disorders

INCIDENCE OF FLATULENCE	PER CENT
Chronic Stomach Bubble	70.5
Colitis	49.7
Redundant Colon	46.7
Hypertension	46.5
Diarrhea	41.0
Belching	38.6
Neurosis (all functional dyspepsias)	35.0
In unselected cases (general incidence)	33.4
Constipation	28.8
Cholecystitis	28.6

Despite a careful consideration of these factors, we found no evidence that either sex, body habitus, or gastric acidity, affected the incidence of flatulence. On the other hand certain clinical conditions shown in table II seemed to bear a definite etiologic relationship to the incidence of intestinal gas accumulations. Some of these factors will be discussed in detail later.

Etiology—The etiology of flatulence may be considered under the following heads:

A. Excessive gas intake or production.
   1. From atmospheric air.
   2. From food decomposition.
   3. From abnormal bacterial flora (intestinal infection).
   4. From the blood.

B. Deficient gas expulsion.

C. Deficient gas absorption.
   1. From interference with intestinal blood supply.
   2. From interference with mucosal integrity.
   3. From interference with intestinal muscular tone.

A. Flatulence Due to Excessive Gas Intake or Production.

Ingested carbon dioxid, as in charged beverages, is either quickly belched, or rapidly absorbed, even from the stomach. It is therefore not likely to produce flatulence.

Rôle of Atmospheric Air—This has long been known to cause flatulence. Its rôle may be considered under the following circumstances of clinical interest:

Air is introduced into the stomach abnormally by air swallowing, air sucking and neurotic belching (Wyllie[39],) (Kantor[18].) The net result of all these procedures is an increase in the air in the stomach and secondarily in the intestine as well. The consequent degree of flatulence really depends on the relative patency to gas of the cardia in the retrograde, and of the pylorus in the physiologic, direction.

Thus in the "chronic stomach bubble" a condition apparently due to spasm of the cardia in the retrograde direction, gas is continually present in the stomach in large amounts as can be readily determined both by physical examination and roentgenologically (fig. 2). There being no way for the gas to escape upward, it has to go through the pylorus and flatulence results. In our series of chronic stomach bubble cases flatulence was present in 70%. Although the condition of chronic stomach bubble is not common—it occurred in 27 of 1533 x-rayed patients (1.76%)—it must be regarded, when it does occur, as one of the most clean-cut causes of intestinal flatulence.

Another type of flatulence of interest in this connection is that encountered after operations. The most recent analyses of intestinal gas from post-operative cases, as performed by McIver[26], show that the composition of the flatus is such that it resembles air modified by interchange with the blood gases. This observer concludes that swallowed air plays an important rôle in the production of postoperative distention. Possibly other factors to be discussed later also enter into the etiology of this disorder.

Self-inflation or auto-inflation is a condition that has long intrigued the medical profession. Many observers regard it as due to air swallowing or air sucking by neurotic or hysterical subjects. It can take place quickly as in the case of the malingerer described by Magendie[23], and may be relieved by gas passage either at will, or under hypnosis, as v. Noorden[39], has reported. Here again, however, other factors than swallowed air must be considered.

Rôle of Food—Flatulence is ordinarily associated with a preponderatingly vegetable diet, the degree of gas formation being in inverse proportion to the utilization of the carbohydrate. Thus such articles as white bread, fine cereals, dextrin, and sugar produce very little gas, whereas pumpernickel, the cabbage family (broccoli, brussel sprouts, cauliflower, kale, kohlrabi, sauerkraut and slaw), turnips, carrots, beets and legumes (peas, beans and lentils) are well-known causes of flatulence.

As already mentioned, pure sugars and starches are digested to the stage of monosaccharids and are absorbed as such. It is conceivable that under

FIG. 2. Chronic stomach bubble. Appearance 9 hours after barium meal.

pathologic conditions a certain amount of further bacterial decomposition may take place, but unless some other gas than CO_2 is produced not much flatulence would result.

It is the cellulose-rich vegetables, namely, those in which the starch granules are enclosed in tough cell membranes, that cause trouble. This is so because, as already stated, specific bacterial action in the ceco-colon is the only method available for the decomposition of cellulose. As a result of this action there are produced various fatty acids, such as formic, acetic, lactic, succinic, valerianic, as well as CO_2, H_2, CH_4, (Schmidt and v. Noorden[30].) The amount of gas evolved is probably considerable, for Schwartz[32] found that if 100 grams of cellulose were completely decomposed at 38° C., they would yield:

CO_2	19.5 liters
CH_4	7.5 liters
H_2	4.0 liters

or 31 liters of gas in all. It need hardly be pointed out, however, that, as everyone knows from stool examinations, the digestion of cellulose is never complete in man.

Furthermore, certain vegetables, such as cabbage, radishes, onions and garlic contain allyl sulfid and allyl mustard oil. Even while cooking they split off certain odorous and possibly toxic gases such as hydrogen sulfid and methyl mercaptan.

Proteins do not produce such large amounts of gas as do the carbohydrates. The former split off the inflammable gases, CH_4 and H_2, and in still smaller degrees, H_2S and NH_3. In many subjects, particularly in those suffering from colitis, the ingestion of raw whole milk is associated with an annoying flatulence. This was found by Ruge[29] to be due to hydrogen, presumably from the milk protein. McIver found 33% of this gas in the flatus of patients on a milk diet.

If there is much delay in the colonic transit of proteins, stinking gases such as skatol and indol may be produced. It should be borne in mind that certain of the odorous gases are capable of absorption into the blood and of excretion through the expired air. Thus, for example, H_2S is 4 to 5 times as absorbable as O_2 (see fig. 1), and according to some (Lauder Brunton)[6], the former gas may actually appear in the expired air. Since this phenomenon obviously furnishes the physical basis for halitosis it would be extremely interesting to secure exact information as to what gases are responsible for the odor of the breath in this condition. Unfortunately no such studies appear to have been made as far as we can learn. That most of the fetid intestinal gases are probably deodorized during their passage through the liver is pointed out by Alvarez who found that as long as an experimental rabbit is kept alive, the bowel gives off no odor and the breath is not offensive, but that as soon as the animal is dead, the stench from the cecum becomes annoying. This is in line with an early observation of Herter and Wakeman[17], that the hepatic, renal, and intestinal epithelial cells have the power of absorbing considerable quantities of indol and of combining it loosely in such a way that this substance cannot be recovered by distillation. It is interesting to spec-

ulate whether some of the heavy breath of liver insufficiency may not possibly be due to the failure of hepatic deodorization of odorous intestinal gases.

Clinically, putrid intestinal gases are often associated with alcoholic dyspepsias (note the breath) as well as with the decomposition of protein-containing exudate in cases of severe catarrhal or organic disease of the intestine (Strassburger)[34]. In general, the expulsion of foul flatus suggests a more severe form of intestinal indigestion than does that of odorless gas.

Rôle of Abnormal Intestinal Flora—It is possible to have flatulence in the presence of a normal or even a specially restricted diet provided the intestinal flora is sufficiently abnormal. Such conditions obtain when large amounts of yeast cells are introduced as in the present vogue of yeast therapy. A more grave situation of this sort is encountered clinically in the case of persistent intestinal infections with presumably pathogenic bacteria. It is only necessary to recall the varied types of carbohydrate fermentation exhibited by the numerous intestinal bacilli of the colon and dysentery groups to appreciate the part played by these or similar organisms when they form the basis of a chronic intestinal infection. The classic studies of Herter[16] will be recalled in this connection. He believed that in the "chronic saccharobutyric type" of intestinal putrefaction of adults, the activity of B. aërogenes capsulatus and of B. putrificus resulted in the production of the large amounts of H_2 and of CO_2 characteristic of this condition, whereas in the "indolic type" of chronic excessive intestinal putrefaction in children, the large amounts of indol produced were probably due to the invasion of the small intestine by certain strains of colon bacilli.

Rôle of Gas Secretion from the Blood—We have seen that gas passage through the intestine is a reversible reaction and that under certain circumstances gas may flow from the blood into the intestinal lumen. It is believed that normally this type of reaction is probably inconsiderable. The question naturally arises, "Is gas secretion from the blood ever of clinical importance?"

In this connection the work of McIver[25] again assumes particular interest. He observed that when either oxygen or hydrogen was injected into isolated loops of small intestine there was a progressive replacement of the absorbed gas by the blood gases, but that in each case, the greatest amount of new gas found was not oxygen or carbon dioxide, which exist in such large proportions in the blood, but nitrogen. This phenomenon is due not only to the fact that nitrogen occurs in the blood under a partial pressure of about 4/5 of an atmosphere (i.e. under a very high tension as compared with that of oxygen which is about one-fifth of an atmosphere), but also because this entire amount is held only in the form of a loose solution in the blood plasma whereas both the oxygen and the carbon dioxide exist almost wholly in chemical combination with the hemoglobin of the red cells. In other words the nitrogen is free to come out of the blood when the condi-

tions are proper. What, then are these favorable circumstances? Even a cursory review of the clinical field reveals several conditions that might favor the secretion of gas from the blood into the intestine. Thus, we would again call attention to the sudden development of flatulence or meteorism in such pathological entities as injuries or diseases of the spinal cord with involvement of the suprasegmental (upper motor neuron) fibers (so-called neurologic ileus); toxic or paralytic postoperative ileus; severe intoxications as pneumonia and typhoid fever; and possibly, some of the hysterical states commonly regarded as being associated with auto-inflation. It may reasonably be assumed that in all the above named conditions there is a sudden drop in intraintestinal pressure, due to some sort of interference with the normal nerve control of intestinal tonicity.

Postponing for the present the discussion of the probable mechanism of this neurogenic atony, we would like at this point to draw an analogy between the sudden *local* drop in pressure in the lumen of the intestine in the cases above mentioned, and the phenomena associated with a sudden *general* drop in atmospheric pressure in caisson workers and divers. As is well known, the symptoms of caisson disease follow too rapid a decompression of the patient, with a resulting evolution of blood gases, particularly nitrogen, throughout the blood and body tissues. Thus, in a fatal case of "the bends" Erdman[11] found in an analysis of gas from the right heart 80% of nitrogen and 20% of CO_2.

According to the view offered, intestinal flatulence may be regarded as a regular accompaniment of suddenly diminished intraintestinal pressure, or in other words a sort of "intestinal bends." The recovery of gas resembling the composition of atmospheric air could well be explained on this basis, since its chief constituent, nitrogen, would naturally predominate in any effort at striking a balance in gas tension between the blood already in equilibrium with the nitrogen of the outside air, and the suddenly created potential vacuum within the intestinal lumen.

There is to be sure, nothing original in this theory. It is but a revival, in modern dress, of the ancient notion of 'pneumatosis" which was advocated one hundred years ago by Graves[15] and subsequently by Trousseau[36]. A generation ago Evans[12] basing his opinion on Ewald's observation that the gas of typhoid meteorism was over 90% nitrogen, concluded "that the presence of large proportions of (this gas) in the mixture of gases contained in any viscus does not necessarily imply that the origin of that gas is the atmospheric air." Among contemporary contributions to the secretion theory of flatulence, Crookshank's essay[8] is perhaps the best known to English readers.

B. Flatulence Due to Deficient Gas Expulsion.

Deficient gas expulsion seldom leads to flatulence except in cases of well-established intestinal obstruction. Thus in constipation our figures show that there is actually a diminished rather than an excessive incidence of flatulence, this symptom occurring in 20 per cent. of constipated patients, against a general incidence of 33 per

cent. With these low figures must be contrasted the high incidence of flatulence in redundant colon (46%). We believe that this increase can be best explained by the mild and transient relative obstructions (spasms) which so often occur in the long loops of reduntant intestines (see fig. 3).

C. Flatulence Due to Deficient Gas Absorption.

This important cause of flatulence may be considered under the following heads:

1. *Interference with Mucosal Blood Supply*—An insufficient blood supply to the mucosa may result from a complete or partial volvulus; from portal obstruction; from mesenteric occlusion (thrombus, embolism, arteriosclerosis); and from general circulatory failure.

Experimentally, Kato[21], and more recently McIver[25] showed that if a loop of small intestine is filled with CO_2 about 90% is rapidly absorbed provided the portal vein is free. If however, the portal vein is ligated only 40% of the gas is taken up in the same unit of time. On the other hand it has been pointed out that such interference with the blood supply as is produced in the above experiment is extremely unlikely to occur clinically. Indeed, Schoen[31] believes that the flatulence attributed to defective circulation might be better explained on other grounds. He admits, however, that interference with the blood supply of the colon is much more serious than with that of the small intestine because vascularization is far less liberal in the former than it is in the latter organ.

Despite these objections we believe that there is considerable clinical support for the impression that flatulence may be caused by defective circulation. In the first place we are all too prone perhaps to underestimate the circulatory demands of the act of digestion. Ordinarily, at least, we are not accustomed to regard the digestion of a meal as a load on the cardiovascular system in the same sense, for example, as we regard the ascent of a flight of stairs. Yet it is the circulating blood that supplies the energy for the motor activities of peristalsis, the physical basis for the secretion of digestive juices, the thermoregulating mechanism for bringing foodstuffs of all degrees of cold or heat quickly and insensibly up or down to body temperature, and finally it is the circulation that furnishes the very vehicle for the removal, by absorption, of the products of digestion. It should not be so strange therefore that one of the first signs of a failing circulation may be the inability to remove intestinal gases. Alvarez quotes Stewart to the effect that differences in the tension of blood gases developing shortly after the onset of auricular fibrillation can upset the gas balance in the bowel wall even before venous stagnation has developed.

The association of flatulence with hypertension is a striking finding. In our series of cases this symptom occurred in almost one-half (46.5%) of the subjects with high blood pressure. The exact significance of this phenomenon is not clear. Flatulence is generally regarded as a common occurrence in arteriosclerosis, particularly in mesenteric arteriosclerosis. In

FIG. 3. Gas caught in loops of redundant colon. Appearance 24 hours after barium meal.

one case of proven coronary artery disease with probable mesenteric arteriosclerosis the gas passed by rectum was so rich in H_2S that it turned silver money in the patient's pockets black from the deposit of silver sulfid. In the syndrome described by Ortner[28] as dyspragia intestinalis intermittens angiosclerotica, a peculiar "quiet" distention (so-called "dead meteorism") of the ascending and transverse colon is associated with the characteristic painful siezures. The anatomical basis for the condition is assumed to be an arteriosclerosis of the superior mesenteric artery, leading to possible angiospastic closure of the vessel or its branches.

It has frequently been pointed out, but may here bear repeating, that flatulence is a cause as well as a result of cardiovascular embarrassment. Thus not only does the elevation of the diaphragm produce mechanical pressure on the heart, but, according to Friedrich Kaufmann[22], any increase in the intradominal pressure may cause a rise in the arterial tension through mechanical factors influencing the distribution of the blood. Hence it is easy to see how a vicious circle may be established.

Interference with Mucosal Integrity—It would appear reasonable to believe that when the intestinal mucosa is damaged by inflammation or ulceration, or its surface diminished by overproduction of mucus there would be increased difficulty with gas absorption and flatulence would result (see fig. 4). Our own experience strongly confirms this view, since colitis was found to be the most common important clinical condition (the chronic stomach bubble being excluded because of its rarity) in which flatulence was encountered (see table II). Indeed, it is possibly the presence of intestinal gas that gives rise to the well-known "belly-consciousness" complained of by these patients.

Contrary to the above clinical experience, Schoen opposes the view that mucosal inflammation causes flatulence and bases his opinion on experimental evidence. He poured corrosive fluids into the small intestine and found no interference with gas absorption. However, it is conceivable that repetition of his experiments, utilizing the large intestine instead of the small, might give results less at variance with clinical experience.

It may be of interest to recall that about 20 years ago the late Dr. Seymour Basch of New York reported two analyses of gas specimens derived directly from the rectum of a case of chronic colitis ("chronic recurrent dysentery"). His findings, obtained on separate days, showed respectively:

a. CO_2, 4.1 per cent.; O, 8.4 per cent.; C_nH_m, absent, H, 8.4 per cent.; 79.1 per cent.; and H_2S, absent.

b. CO_2, 3.5 per cent.; O, 18.4 per cent.; CH_4, 5.1 per cent.; H, 0.4 per cent.; N, 72.6 per cent.; and H_2S, absent.

Basch felt that the oxygen figures in the second analysis may have been too high owing to possible air admixture in the rectal tube that was used. Somewhat similar figures are recently reported by McIver[26] in a case of diarrhea.

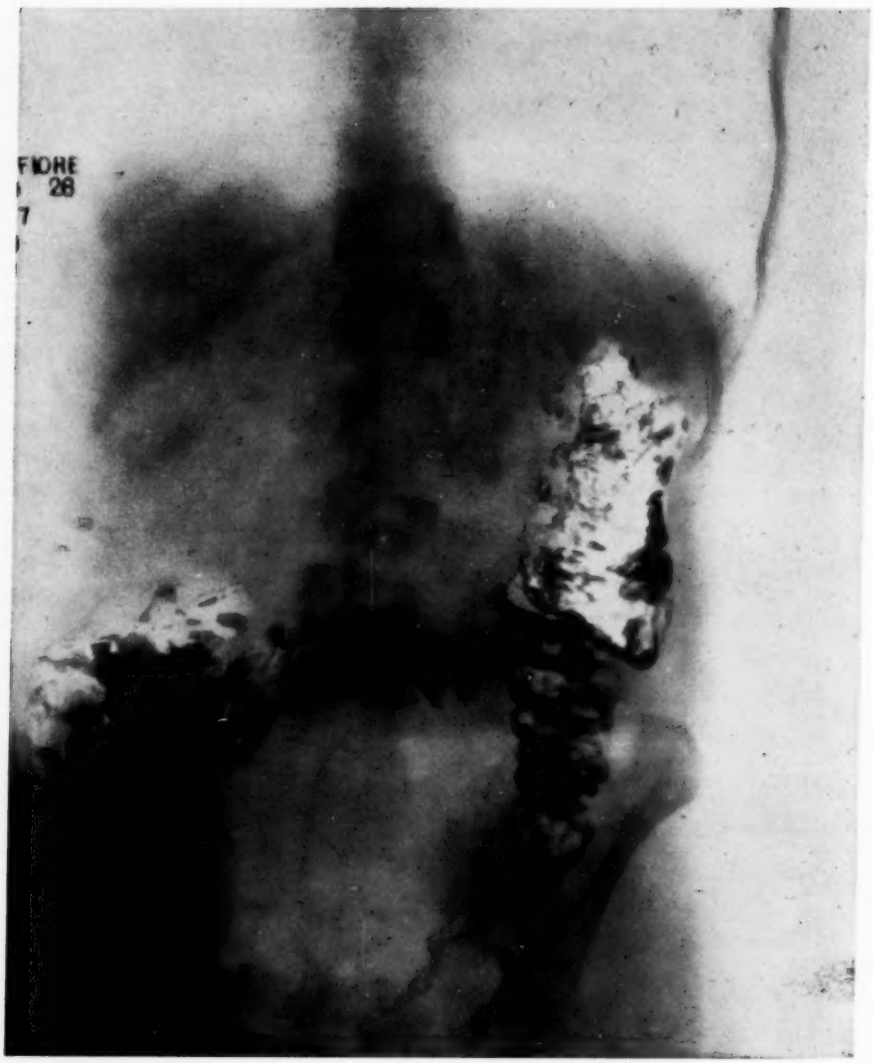

FIG. 4 Gas at splenic flexure in a case of probable tuberculous colitis. Appearance 9 hours after barium meal.

Interference with Muscular Tone (Intestinal Atony)—The present trend of opinion seems to emphasize intestinal atony as a prime factor in the production of flatulence.

The form of this theory that most appeals to us is the following:

When for any reason the intestinal muscular tone is impaired, the lumen of the gut enlarges. This immediately lowers the intraintestinal pressure so that not only is gas absorption diminished but the possibility of gas excretion from the blood is enhanced. Soon a vicious circle developes since the greater the accumulation of gas the greater the depression of muscular tone due to stretching. This is particularly true if some of the gas locally produced is neuro- or myotoxic in nature. In this connection, Schoen mentions the tremendous depressing effect of certain amines derived from intestinal digestion, while McIver[25] reports a marked but transient drop in blood pressure from the intestinal injection of the highly absorbable H_2S.

The mechanism of intestinal atony in general is nowadays best explained on a neurogenic basis. It is believed that a characteristic depression of muscular tone results from some form of abnormal irritation of the inhibitory splanchnic nerve fibers. For example, adynamic or paralytic—i.e. non-obstructive—ileus is assumed to be due to such splanchnic irritation, because it has recently been shown that the ileus may be overcome by simply breaking the sympathetic reflex arc. This can be accomplished by anesthetizing either the (sensory) spinal nerve roots (Wagner)[38] or the (motor) splanchnic pathways (Ochsner)[27].

Similarly, intestinal atony may result from even more remote nervous disorders. Thus, in disease or injury of the spinal cord involving the suprasegmental visceral nerve pathways, the lower (segmental) fibers are released from superior control. When this occurs the normal balance between the inhibitory (sympathetic) and excitory (autonomic) innervations is assumed to be upset in the sense that it is the sympathetic influence that predominates (Feltkamp)[13]. Accordingly, whenever the intestinal distribution is involved, ileus with meteorism develops. Whether this theory be accepted or not, meteorism is known to be a striking complication of such upper cord conditions as trauma, syringomyelia, combined sclerosis, and pernicious anemia. Elsberg [10] has pointed out the occurrence of ileus following laminectomy in the lower dorsal region.

That the nerve pathways are fundamentally concerned in the development of meteorism in such toxic states as peritonitis, typhoid fever, pneumonia,* and general sepsis, is more than probable. Similarly, a neurogenic mechanism may be safely assumed to underlie the hysterical form of pneumatosis such as that described many years ago by Valentiner[37]. Whether or not the lesser forms of distention more commonly encountered in practice are of neurogenic origin is not yet definitely established, although the fact that flatulence occurs most often when patients are fatigued or emotionally unbalanced seems to lend obvious support to such an hypothesis.

*For gas analysis of intestinal flatus in distended pneumonia patients see McIver[26].

III. Therapy of Gas in the Intestine.

Nervous Factors—Flatulence, as well as bowel troubles in general, is known to be commonly associated with nervous and mental symptoms. Indeed, owing to the nature of the disability, patients are often prone to be unduly depressed and morbid over their condition and to exaggerate what they regard as their repulsiveness to society. On the other hand this symptom may be but an expression of a more general neurosis. Its onset may at times be abrupt, following a psychic shock or trauma.

Since flatulence is, in this sense, a functional condition, treatment must be planned on a sufficiently comprehensive basis. This implies attention to such major hygienic measures as regular habits of living, rest and recreation. Psychic and emotional rest is particularly important, but this is not always easy to bring about, despite much patient and reassuring encouragement on the part of the physician. Perhaps the most satisfactory medication for the general treatment of flatulence is a mild sedative—we use a bromid and chloral mixture—which may have to be continued for long periods. Carminatives also, we believe, have their place in the mild cases.

The beneficial effects of hydrotherapeutic measures should not be forgotten. Hot moist applications relieve spasm and favor effective peristalsis. The wet abdominal compress as used by Baruch[3] may prove useful in appropriate cases. Trousseau, according to Crookshank, favored cold affusions and ether.

In those individuals who exhibit a spasmophilic or vagotonic makeup, belladonna or its alkaloid, pushed if need be to the point of cycloplegia, is very helpful. In Balint's "tympanismus vagotonicus" [2] the abdominal distention is said to be removed by atropin and reproduced by physostigmin. However, as will be seen directly, physostigmin itself is sometimes of decided benefit in this condition. Thus, in neurologic ileus, where the distention is due to injury or disease of the spinal cord, injections of physostigmin or of pituitrin (see below) possibly constitute the best treatment now available. The use of these drugs in toxic distentions (pneumonia, typhoid, sepsis, late intestinal obstructions) though less likely to be followed by relief, is also to be recommended. Pilocarpin is sometimes useful; it acts in the same way as physostigmin, by stimulating the autonomic fibers. The antidote to both these drugs is atropine.

Air Swallowing—Most air is introduced into the stomach by neurotic belching. Patients afflicted in this way should be taught the difference between voluntary belching, which always introduces some air into the stomach, and spontaneous belching, which expels air only; and they should be directed to control the former habit. In paroxysmal belching, or in air sucking (cribbing), having the patient bite on a large cork may break up the attack. General sedatives are of course indicated.

In our patients with chronic stomach bubble, it was found that gastric hyperacidity occurred fairly often. In some of the cases, alkalies seemed to

break up the spasm, in others belladonna, but many proved refractory to treatment. In such obstinate cases, forcible dilatation of the cardia might be considered, though it may with justice be objected that the cure is worse than the disease.

Diet—Not much need be added to what has already been stated or implied in the text that has preceded. Avoidance of an excess of cellulose and the careful selection and cooking of vegetables should take care of all ordinary requirements. In some individuals raw whole milk should be entirely eliminated from the diet. For the majority of cases, a full well-balanced regime, such as an expanded Schmidt diet, suffices. Fluids at meals, especially those that can be drunk quickly, should be avoided, in order to minimize air swallowing.

In patients requiring more active treatment, a preliminary dose or two of castor oil is desirable to clear out old residues. Possibly a day of starvation may be interposed before feeding is resumed. The amount and type of food depends on the degree and nature of the flatulence. In patients with particularly foul flatus, a course of acidophilus milk in increasing doses seems now to be the best initial procedure. The diet may then be built up gradually as in the usual management of putrefactive intestinal dyspepsia. Similarly, cases of fermentative dyspepsia will respond in their turn to appropriate dietetic procedures.

Post-Operative Distention—As regards the prophylaxis of post-operative distention, we quite agree with Alvarez that it is time to discard the ancient practice of purging patients routinely as a preparation for surgical intervention. In addition, too long a period of pre-operative starvation is unnecessary.

The simplest treatment for post-operative distention resulting from air swallowing, is postural, the object being to encourage spontaneous belching. This may be accomplished, in favorable cases, (1) by putting the patient into as nearly an upright position as his wound will permit, and (2) by turning him on his left side and thus bringing the cardia uppermost. If these measures fail, a tube should be passed into the stomach for the purpose of puncturing the stomach bubble. Intubation with a large tube (size 36 to 40 F.) of the proper consistency is a speedy and perfectly safe procedure in the hands of an experienced operator. This form of treatment has the additional advantages of removing obnoxious fluids from the stomach and of permitting rapid and thorough lavaging. The intubation may of course be repeated at appropriate intervals.

When the gas accumulation is principally intestinal, the mere introduction of a rectal tube suffices to relieve many patients whose difficulty is due to ineffectual abdominal wall contraction. In most cases soothing oil injections are preferable to irritating enemas. When the meteorism appears to be due to intestinal atony, the best results, according to some, are obtained from drugs which increase smooth muscle tonus. Pituitrin, 0.5 to 1.0 c.c. by deep intramuscular or hypodermic injection is perhaps the most com-

monly used medication. It is often advisable to follow the injection in about half an hour by a large enema (2 quarts) to increase the intestinal contents and thus aid the expulsion of gas. The use of physostigmin salicylate in doses of 1/40 to 1/20 grain has given good results in actual practice. The careful observations of Martin and Weiss[24] showed that the larger doses (up to 1/16 grain), administered intramuscularly, proved successful in relieving otherwise rebellious cases of non-toxic abdominal distention. Gas was belched or expelled from the rectum within 10 to 40 minutes after an effective dose was given. They saw no cardiac depression in even desperately sick patients. Pilocarpin hydrochlorid, in doses of 1/12 grain hypodermically is also said to be of value. Schoen has shown experimentally that CO_2 absorption is promoted by the increase in intestinal tone that accompanies pilocarpine administration.

In contrast to the above recommendations, McIver[26] warns against drugs which increase peristalsis in postoperative distention, and favors the use of morphine to quiet intestinal movement. Finally, the successful results following both spinal and paravertebral anesthesia in paralytic ileus should be borne in mind. They have already been mentioned in the section on the mechanism of intestinal atony in this and similar conditions.

Constipation — Although flatulence is not a troublesome complaint in simple cases of constipation, gas formation may be definitely increased after the initiation of a rough, stimulating diet. Fortunately this condition usually subsides spontaneously after the new regime is established, or at the most, after administration of a mild sedative mixture, or an occasional saline enema.

In constipation due to redundancy of the colon, flatulence is much more likely to be a troublesome feature. Once the situation is correctly appraised, the gas distress usually responds to appropriate treatment [19].

Colitis—In cases of simple colitis, that is, colonic irritability not associated with infection or ulceration, the flatulence yields to simple measures. In our experience appropriate simplification and regulation of the diet, mild sedatives, and sometimes belladonna, constitute an effective therapeutic program. In addition, as described elsewhere [20], we prescribe half-ounce or ounce doses of a mixture of equal parts of barium sulphate and kaolin once or twice daily in fermilac, cocoa, or thick cereal, according to the preference of the patient. These inert powders seem to depress mucosal irritability and thus aid gas absorption. It is possible that large doses of loose charcoal would act in similar fashion although we have not tried this, and have obtained an impression of uniform failure from the use of the more or less compressed charcoal tablets commonly employed by patients.

In flatulence associated with gastrogenous entero-colitis, whether due to achylia gastrica or following extensive gastric resections, the administration of hydrochloric acid in appropriate dosage, is often helpful.

In cases of colitis gravis, such as those characterized by infection (fever) and ulceration (hemorrhage), the same treatment appears indicated as has been outlined for simple colitis. However, we have never been able to satisfy ourselves that the welcome remissions that occasionally punctuate the course of this distressing disorder could be ascribed to any of the therapeutic measures we have employed.

Cardiovascular Insufficiency — In cases of general heart failure the best treatment for the flatulence is obviously the control of the cardiac condition. This means, ordinarily, rest and digitalis. Under the head of rest however, the important idea of digestive rest should not be neglected. This is carried out by a proper restriction and simplification of the diet. In very sick or edematous patients who take milk well, the Karrel diet is often sufficient to control the flatulence adequately. In other cases the ordinary convalescent ulcer diet or the Schmidt intestinal diet proves satisfactory. All these regimens are based on the principle of frequent small feedings of readily digestible foodstuffs, and thus automatically avoid the sudden excessive demands on the digestive circulation produced by the usual large repasts.

The flatulence associated with high blood pressure, as well as with arteriosclerosis with or without hypertension, is also treated by rest of the digestive tract. Here one must observe the principle of split feedings with foods least likely to produce gas, and the patient should be further cautioned to rest and relax an appreciable time before, and particularly after, eating. Failure to take these precautions may result in anginal attacks or, in cases of advanced coronary arterial disease, in a fatal seizure.

In patients with cardiovascular disabilities the control of constipation is important. However, inasmuch as the usual rough diet is absolutely contraindicated, recourse must be had to the freer use of cathartics. If mineral oil works well, the problem is solved. Otherwise an effective and popular procedure is the administration of a saline cathartic. This is best given in concentrated form on a fasting stomach and should be followed immediately by a glassful of water. Breakfast should be delayed for at least half an hour. Both the flatulence and the increased blood pressure often respond well to this treatment. Cures at the popular spas are sometimes followed by relief for considerable periods.

For the acute distentions and recurrent painful seizures of dyspragia arteriosclerotica, diuretin (theobromin sodium salicylate) is recommended by Ortner and by v. Noorden[30]. The dose is 0.5 gram three times daily for months at a stretch. We have had no experience with this medication.

Carminative Treatment — Carminatives have long held a place in the treatment of flatulence. Just how they act is not clear, though they seem effective in many mild cases. Their influence, presumably reflex, is said to be slightly cathartic, yet at the same time mildly anesthetic and antispasmodic.

Perhaps the most useful types of carminatives, as shown by long experience are:

Group 1. Ether, chloroform, the volatile oils, and the concentrated alcoholics. Examples are: spiritus aetheris (one teaspoonful), Hoffman's anodyne (one teaspoonful), spiritus menthae piperitae (5 to 20 drops), crême de menthe, cointreau, Benedictine, etc. A favorite hospital prescription, according to Bastedo[5] is:

R/ Compound spirit of ether
Aromatic spirit of ammonia
Compound tincture of lavender
Spirit of chloroform
aa 15 minims

Group 2. Herbs or teas, as in the following continental prescriptions (Strassburger)[14]:

R/ Semen foeniculi
Fruct. anisi
Fruct. cari
Folia menthae pip. aa 25.0
M.ft.pulv. Sig. Brew into a tea, one tablespoon to each cup of water.

R/ Cinnamon
Ginger aa 35.0
Nutmeg
Cardamom aa 15.0
M.ft. pulv. Sig. 1.0 to 2.0 as needed.

Group 4. Carminative enemas. The following combinations are used (Bastedo): Oil of turpentine, one-half ounce, or tincture of asafetida or spirit of peppermint, 1 dram, added to a soapsuds enema or to 8 ounces or more of infusion of chamomile.

General Results of Treatment—On the whole the treatment of flatulence as outlined above, is satisfactory. Our chief failures were observed in cases of intermittent attacks of gas distress for which we could find no adequate reason. In some instances these attacks occurred in obviously sensitive persons and could then be attributed to an excitability of the involuntary nervous system that we were unable to quiet. In other cases the patient seemed placid enough, yet the attacks persisted despite all we could do to control them. The abdominal films of one such case showed several large dense shadows of calcified mesenteric glands. It is conceivable that these masses acted as foci of irritation to nerve pathways and thus brought on the attacks of gas. Further observations along these lines are obviously desirable.

IV. Summary

1. Intestinal flatulence ranks third among the ten most common complaints of private patients suffering from digestive disorders.

2. In general, flatulence may be caused by excessive gas intake or production, by deficient gas expulsion, or by deficient gas absorption.

3. Atmospheric air plays a definite but not necessarily a major rôle in the etiology of flatulence.

4. The chronic stomach bubble is a rare but striking cause of flatulence.

5. The diet may cause flatulence, but this factor can be readily controlled in most cases.

6. An abnormal intestinal flora plays the leading rôle in the flatulence of intestinal infections.

7. Gas may be secreted from the blood under certain circumstances. At times, this may be an important cause of flatulence. Evidence is presented

for the belief that the greater part of the gas so secreted is nitrogen.

8. Flatulence from deficient gas expulsion arises in complete obstruction and in redundant colon. Constipation is not a frequent cause of flatulence.

9. Deficient gas absorption is an important cause of flatulence. It may result from interference with mucosal blood supply, destruction of mucosal integrity, or depression of muscular tone.

10. Interference with mucosal blood supply occurs in volvulus, portal obstruction, mesenteric vascular occlusion or sclerosis, and general circulatory failure. The incidence of flatulence in hypertension was strikingly high (46%) in our cases.

11. Interference with mucosal integrity is best illustrated in colitis. Almost one-half of our colitis cases showed flatulence.

12. Interference with muscular tone (atony of the intestine) is probably a very important cause of flatulence. Atony may result from various neurogenic or myotoxic causes and thus retard gas absorption and favor gas excretion from the blood.

13. In our opinion, a theory of flatulence which would assume a sudden development of intestinal atony with rapid filling of the bowel by blood gases, chiefly nitrogen, would best account for many of the sudden baffling distentions encountered clinically.

14. Such a theory would explain the flatulence of neurologic ileus; of toxemias associated with severe pneumonia, sepsis, and typhoid fever; of various hysterical states; as well as that encountered post-operatively.

15. The treatment of the more important clinical types of flatulence is discussed.

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Lung Volume and Its Variations*†

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THE statement that respiratory exchange in the lower branches of the bronchial tree, the bronchioles and the alveoli is carried on chiefly by diffusion, is probably correct up to a certain point. However, the importance of respiratory movements in the ventilation of the air sacs cannot be relegated to a rôle of minor importance. Without such movements the respiratory function fails to support life even under artificial conditions of enormously increased diffusion pressures. The efficiency of the ventilating system inaugurated by the respiratory movements is obviously most important in abnormal pulmonary conditions.

On approaching the subject of pulmonary ventilation it is necessary to describe briefly certain terms in common use in order that no confusion of definition may arise. For our present purpose six such definitions are necessary,—

a. Vital Capacity—The volume of air expired by a maximum expiration after a maximum inspiration;

b. Residual Air—The volume of air remaining in the lungs after a maximum expiration;

c. Total Lung Volume—The sum of (a) and (b) or the total capacity of the lungs at the end of a maximum inspiration;

d. Middle Capacity—This term is applied to that quantity of air which is in the lungs if the breathing be stopped midway between an average resting inspiration and expiration.

e. Functional Residual Air— By this term is implied the amount of air which is in the lungs at the end of an average resting expiration. It would consist of the residual air as described in (b) plus the volume of air represented by the volume expelled from the lungs between an average resting expiration and a maximum expiration, or what is known as the (f) reserve air.

Of these measurements the vital capacity and the reserve air can be readily determined and this by an ordinary spirometer. The measurement of the total lung volume, residual air, and functional residual air can only be determined by a more complicated method such as that described by Van

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Slyke and Binger.[1] We have used such a method. The principle of this method depends upon the breathing of a rich oxygen mixture containing an accurately known quantity of hydrogen approximating the volume of nitrogen in the lungs at the time of the beginning of the determination. After some minutes of breathing through a closed circuit there is a thorough mixing of the hydrogen and nitrogen in the lungs as well as the rest of the circuit. The percentage concentrations of H_2 and N_2 are then determined. Since

$$\frac{\text{initial vol. of } N_2 \text{ in lung air}}{\text{initial vol. of } H_2 \text{ in mixture}} = \frac{\text{final \% } N_2 \text{ in mixture}}{\text{final \% } H_2 \text{ in mixture}}$$

$$\text{vol. } N_2 = \text{vol. } H_2 \times \frac{\text{per cent } N_2}{\text{per cent } H_2}$$

But nitrogen constitutes 79.1 per cent of air; therefore, the volume of air in the lungs at the commencement of the determination is

$$\frac{\text{vol. } N_2 \times 100}{79.1}$$

minus dead space in the apparatus. It is necessary, however, to know the exact phase of respiration at which the respiration of the hydrogen-oxygen mixture begins. This is obtained from a tracing taken with a spirometer. In such a tracing may be incorporated the normal respiratory cycle where the estimation is made (fig. 1).

To calculate the total lung volume, that portion of the vital capacity lying above the point at which the estimation was made, is added to the lung volume as measured by the nitrogen-hydrogen ratio. Similarly the residual air is calculated by subtracting that portion of the vital capacity lying below the point at which the estimation was made.

The functional residual air varies, depending upon the relative position of the middle capacity or, in other words, the position in the total capacity of the lungs where average respiration at the moment is taking place. This we know to be changeable not only in different people but in the same person under varying conditions. At the moment sufficient data is not available to discuss these changes in middle capacity but it would seem to change in normals under different conditions of rest and work, of position, of reflex stimuli, and probably many other unknown factors. Until this subject has been more thoroughly investigated it is difficult to arrive at any conclusion as to its influence on pulmonary ventilation.

The efficiency of pulmonary ventilation would appear to rest upon the relationship between the residual air and the total lung capacity. In normal individuals this has been found, by different workers, to vary between 26% and 33%, the variation depending upon the methods used. In our experience with a number of healthy adult males it has been found to average 33%.

On considering the different thoracic lesions which might interfere with pulmonary ventilation, it is possible to divide them into two main classes; first, those conditions which although encroaching upon the total

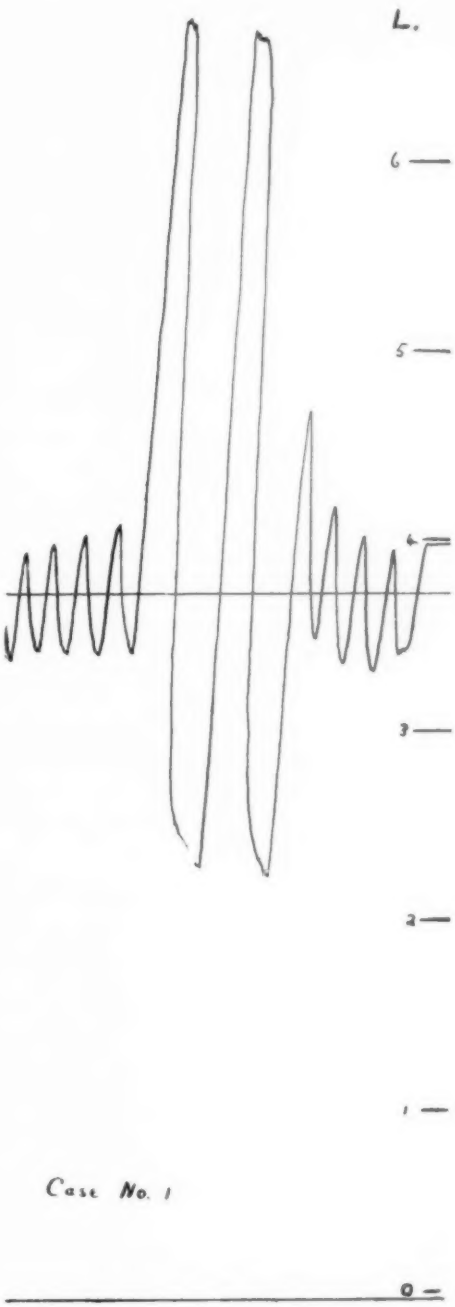

FIG. 1. Normal Case. Tracing of respiratory movements with vital capacity. (a) Point at which estimation of lung volume was started. Numerals represent litres of total lung capacity. From end of forced expiration to base line represents residual air.

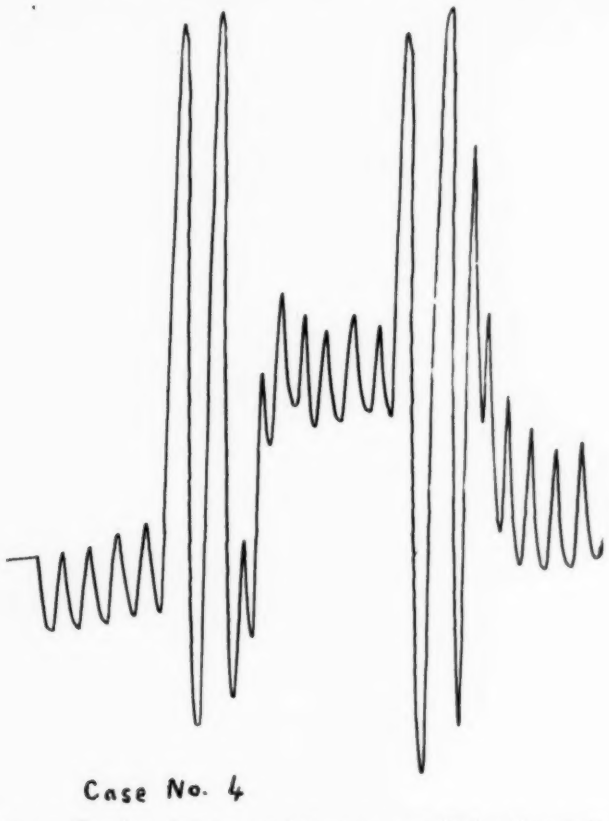

FIG. 2. Tracing showing variations in so-called mid-capacity.

alveolar area of the lung at the same time do not interfere with the expansile power of the uninvolved portions. Examples of such are hydrothorax, pneumothorax, and localized tuberculosis. The second class includes those conditions of the lungs or thorax which interfere either with the expansibility of the lung or the efficiency of the respiratory muscles. Examples of such are found in chronic passive congestion of the lungs due to circulatory failure, chronic emphysema, paroxysmal asthma, and paralysis of the intercostal muscles or diaphragm or severe pleuritic pain. There are a number of conditions which cannot be classified at the moment in either of these categories, such as acute lobar pneumonia, miliary tuberculosis, diffuse bronchiolitis and massive pulmonary collapse.

It has usually been considered that a reduction in vital capacity is an index of the efficiency of pulmonary ventilation. We have found that this is not necessarily the case. It is a common observation that under certain circumstances vital capacity may be considerably reduced but still the individual need not suffer from dyspnea or any respiratory distress. We believe that it depends upon the ratio between the total lung capacity and

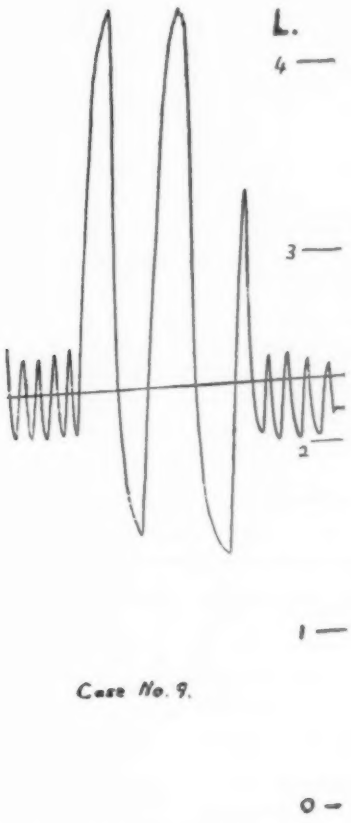

FIG. 3. Case of pleurisy with effusion, left-sided. Legend as in Fig. 1.

the residual air as to whether dyspnea under ordinary conditions will ensue.

We have found in cases of pleurisy with effusion and in artificial pneumothorax where the opposite lung is in good physical condition, that although the vital capacity may be reduced to a pronounced degree, the ratio between the total lung capacity and the residual air remains within normal limits. In such cases there is no dyspnea or respiratory distress within ordinary limits of exertion. Similar observations have been made by Garvin, Lundsgaard and Van Slyke[2] in cases of pulmonary tuberculosis.

In regard to the second category our investigations in cases of circulatory failure have shown a more or less direct relationship between the severity of the pulmonary symptoms and the reduction in vital capacity. This merely confirms the findings of many previous observers. These pulmonary symptoms have been considered in great part to be intimately associated with this reduction. But this explanation could not be reconciled with a similar reduction in vital capacity

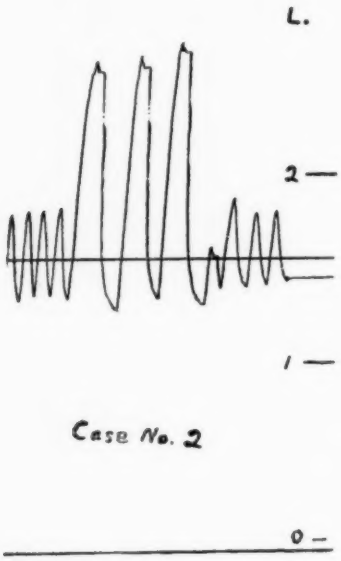

FIG. 4. Case of circulatory failure. Legend as in Fig. 1.

found in category 1 which was not accompanied by respiratory distress. We have found, however, a striking difference in the amount of residual air in these two types of cases. In cases of circulatory failure with a reduced vital capacity, instead of the residual air diminishing proportionately and thus maintaining the same ratio to the total lung volume, the residual air may not only relatively but also absolutely increase. This increase is brought about by a progressive encroachment of the residual air upon the reserve air, so that the unventilated area of the lung at the end of a forced expiration becomes greater and greater. It is not unusual to find in cases of circulatory failure that the reserve air has completely disappeared and that a forced expiration is not any greater than an average resting expiration. We have found that the residual air may amount to more than 50% of the total lung capacity. This corroborates the findings of Binger.[3] It is quite obvious under these circumstances how difficult it would be for an individual so placed to carry on proper alveolar ventilation. We have found that as the respiratory symptoms diminish there is a progressive reduction in the ratio of the residual air to the lung capacity, while as the symptoms increase the converse occurs.

A similar condition of affairs has been found by Lundsgaard and Schierbeck[4] to exist in cases of pulmonary emphysema.

In considering the underlying cause of such a symptom as dyspnea in any individual case we are frequently confronted by a number of intimately connected factors all of which may contribute towards the eventual result. Therefore, we do not wish to over-

emphasize the importance of any one of these factors in its relation to the others, but it seems to us that sufficient attention has not been given to the variations in the relative conditions existing in pulmonary ventilation. Furthermore, in view of the great advances that have been made in recent years in the understanding of the chemical and nervous regulation of respiration, the actual conditions under which the pulmonary function is being carried out have been more or less lost sight of. We merely wish to revive the importance of the pathological physiology of pulmonary ventilation while at the same time keeping it in its proper perspective in relation to the other factors which regulate respiration and pulmonary ventilation.

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A Study of the Effect of Chronic Pulmonary Diseases on the Volume and Composition of the Blood*

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With the phylogenetic development of a hemolymph system, the contact of respiration and circulation became complete. Throughout all the metamorphosis that bridges the gap between primitive organs and the complicated bodily systems of vertebrates, this relationship is maintained, and the mutual dependence of one on the other is strengthened almost in direct ratio to the multiplication of the necessities of complicated processes of life.

These ancient functions of respiration and circulation of blood are so vital and so fundamental a part of life that they are protected by a physiologic reserve far in excess of any requirement that could be anticipated by any of the exigencies of natural life. The body, however, is beset by many agencies that wear down and dissipate physiologic reserve, sometimes of one, sometimes of the other of these two functions. Reserve in the function bearing the brunt of assault prevents disaster. Compensatory factors in the function indirectly affected are ultimately inevitable and serve to stabilize the actions of both. Regardless of handicap, if competency is to be maintained nutrition must be supplied to near and distant parts; oxygen must come to the blood and through it to the tissues.

It has long been recognized that certain changes of a compensatory nature may occur in the blood in disturbance of the cardiorespiratory system especially when normal pulmonary ventilation is impaired. Chronic emphysema, chronic asthma, pulmonary fibrosis, and obstructive conditions furnish the usual clinical examples of conditions which impair the respiratory and circulatory functions. Lowered oxygen tension in the arterial blood, or arterial anoxemia, may induce erythrocytosis as measured by the concentration of erythrocytes in the peripheral blood. This response of the blood is probably common to that occurring in other conditions which produce anoxemia, such as the erythrocytosis which occurs after long residence at high altitudes. Likewise, experiments in the oxygen chamber, under conditions of lowered oxygen tension, have revealed hyperactivity of the bone

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marrow. Recent investigations by Dallwig, Kolls, and Loevenhart, on animals confined at normal barometric pressures but at low oxygen tensions, have emphasized the proportion existing between the degree of anoxemia and the resulting erythrocytosis. The erythrogenesis resulting from residence at high altitudes may not be due entirely to lowered oxygen tension. Other factors have been suggested, such as the effects of lowered atmospheric pressure, of cold, of light, of dryness of the air, of increased loss of water, of rapid evaporation from the surface of the body, of redistribution of the peripheral blood, and of the vasomotor changes. Regardless of these contributing effects, there seems to be no reason to doubt that anoxemia is the exciting factor in stimulating the changes in the blood.

The blood, in clinical conditions accompanied by chronic disturbance of pulmonary oxygenation, has been studied in relation to the concentrations of hemoglobin and erythrocytes in the peripheral blood. Data concerning the circulating volume of blood, plasma, and hemoglobin, and correlative information on the oxygen of the blood are lacking. The work of Smith and his associates, on the effects of short periods of residence at high altitudes, has been studied by means of the dye method for determining volume of blood and of plasma. This condition, however, does not simulate that occurring in diseases in which chronic conditions of anoxemia exist over a period of years. The time seemed apropos for a fuller investigation of the possible changes occurring in the circulation and in the blood in diseases in which chronic anoxemia may be suspected to be present. The problem is of more than academic interest, because frequently the question is raised whether a diagnosis of primary or of secondary polycythemia should be made when, in a given case, erythrocytosis and cyanosis are present.

Material Studied

The following groups of patients were studied:

(1) Twelve subjects with chronic bronchitis and emphysema, associated with significant grades of cyanosis; (2) two subjects with polycythemia vera and splenomegaly, complicated by chronic pulmonary disease, emphysema or asthma and exhibiting excessive grades of cyanosis, and (3) one subject with an excessive degree of cyanosis and who gave evidence of hypertrophy of the right ventricle of the heart with myocardial insufficiency, the clinical diagnosis was Ayerza's disease.

The main study was of the patients in group 1; the patients in the other groups are merely referred to for comparison.

Methods of Study

Concentration of the erythrocytes and hemoglobin was determined in the peripheral blood. A combination of Haden's[4] and Osgood's methods of determining the acid hematin was employed for the estimation of hemoglobin. The volume of blood and of plasma each was determined by the dye method.[7] Congo-red was used and a mixing time of three to six minutes was allowed. The volume of circulating hemoglobin was studied by obtaining the product of the total blood

volume and the grams of hemoglobin for each 100 c. c. of blood. The oxygen content and percentage saturation of the arterial and of the venous blood was determined by the Van Slyke volumetric method. Blood was obtained by arterial puncture of the brachial or of the radial artery. The percentage saturation of hemoglobin in the individual erythrocyte was calculated according to the method of Haden.[5] The vital capacities were determined and charted as the actual and calculated values.

Values for Normal Persons

Hemoglobin—The average normal concentration of hemoglobin in normal persons is 15.6 gm. for each 100 c. c. of blood; this value in males is 16.4 and in females, 14.2. There is a definite difference in the mean values in males and females. In females the mean value for the volume of circulating hemoglobin is 12.2 gm. for each kilogram of body weight, and 442 gm. for each square meter of body area; in males the corresponding values are 14.7 gm. for each kilogram of body weight and 541 gm. for each square meter of body area.

Haden's values for the normal volume and hemoglobin content of the single erythrocyte are as follows: The normal value for the volume index is 1; for the saturation index is 1 and for the average erythrocyte in cubic centimeters is 9.2×10^{-11}. The grams of hemoglobin in the average erythrocyte is 3.12×10^{-11}, or an actual percentage of hemoglobin in the individual erythrocyte of 33.9, with a range of 32 to 36.

Hematocrit values— The normal hematocrit value, using dry sodium oxalate as an anticoagulant, is 42 per cent by cells. This has been shown by Whipple and his associates to be approximately 3 per cent less than the true normal volume obtained by using solution of sodium oxalate as an anticoagulant, the wet method.

Blood volume—The range of volume of blood has been well established in a series of normal subjects, of average weight and height, by Rowntree and Brown. The normal range is from 70 to 97 c. c. for each kilogram of body weight, with a mean value for normal persons, males and females taken together, of 87.7 c. c. As is well known, the variations in body weight in normal subjects are fairly great. When calculated on the basis of body area, the mean value or blood volume for normal persons of both sexes taken together is 3278 c. c. for each square meter of body area. The variations due to slight grades of underweight and overweight is less marked according to body area than according to body weight. The mean plasma volume for normal subjects is 51.2 c. c. for each kilogram of weight, and 1920 c. c. for each square meter of body area. The variations in plasma volume that are coincident with conditions of underweight and of overweight in normal subjects are proportionately the same as the variations in blood volume under like conditions.

The question as to whether blood volume is determined by body weight or body area has been discussed by Dreyer and Ray, and by Rowntree and Brown. Correlation coefficients have indicated a higher correlation of blood and of plasma volumes to body

area than to body weight. For the present, we have expressed the blood and plasma volumes in relation both to body area and to body weight; our deductions have been based largely on the changes found according to weight, as much of the data previously published has dealt with this relationship.

Considerable difficulty is encountered in determining abnormalities in the blood volume in disease of subjects who either are abnormally underweight or overweight. In order to determine whether the changes in blood volume are actual or only apparent on the basis of body weight, we have attempted to obviate this difficulty by expressing the blood volume of the patient according to both his body weight and his body area, and then calculating his blood volume according to his ideal weight for his height and age by actuarial standards. The last value is designated as blood volume according to corrected body weight. Eventually, blood volume may be expressed as plus or minus from zero or normal. This question has been carefully discussed by Rowntree and Brown.

The figure for oxygen capacity of normal blood is 21 volumes per cent. The oxygen capacity of arterial blood under normal conditions is 20 volumes per cent and the percentage saturation, 95.6 per cent. The corresponding values for venous blood are 14.5 volumes per cent and 70 per cent.

The normal vital capacity varies with height, weight and body area. The actual and estimated volumes in the cases studied are given in table 1.

STUDY OF TWELVE CASES IN GROUP I.

Of the twelve cases (table 1) selected for study, one was that of a woman and the others were men. All but four patients were more than fifty years of age; neither obese nor undernourished patients were in the group. The actual weight of each patient compared favorably with the ideal weight for his height and age. The three most striking variations from ideal weight were in cases 2, 3 and 11. In case 3 the weight was 18 kg. more than the ideal weight for height and age, and this discrepancy made a considerable difference in the estimations of the volume of the blood. The same was true in the other two cases, but to a much less degree.

Hemoglobin—The values for hemoglobin that were employed in this study were as follows: (tables 2, 3 and 4) (1) the grams in each 100 c. c. of blood, (2) the grams of circulating hemoglobin for each kilogram of body weight and for each square meter of body area, and (3) the percentage in the individual erythrocyte. The grams of hemoglobin in each 100 c. c. of blood varied from 11.5 to 20 with a mean value of 16.5. In six cases the values were in excess of 16.4 gm. which is the normal value for males. The total amount of circulating hemoglobin was 14.9 gm. for each kilogram of body weight and 554 gm. for each square meter of body surface. In order to determine the percentage of hemoglobin in the individual erythrocyte the volume index first was calculated. The average value for the volume index was 1.05. The saturation index was 1.22, the volume of the average cell was 8.86 c. c. $\times 10^{-11}$. The number of grams of hemoglobin in the average cell was 3.64×10^{-11}. The average value for the actual percentage of hem-

TABLE I.

CLINICAL OBSERVATIONS IN TWELVE CASES IN WHICH THERE WAS CHRONIC BRONCHITIS, EMPHYSEMA, AND SIGNIFICANT GRADES OF CYANOSIS

Case	Complaint	Blood pressure mm. mercury		Vital capacity, c. c.	Thoracic roentgenogram	Electrocardiogram	Clinical observations	Diagnosis	Comment
		Systolic	Diastolic						
1	Asthmatic attacks, dyspnea, orthopnea, cough, sputum	105	80	3128 to 4480	Negative	Rate 63, sinus rhythm, QRS notched in lead III, left ventricular preponderance	Typical emphysema, cyanosis, pleural rub	Emphysema, chronic bronchitis, nasal polyps, sinusitis	Hardened cartilages, nonelastic chest
2	Dyspnea	102	58	3625 to 4735	Negative	Sinus rhythm	Cyanosis, dyspnea, wheezing râles	Emphysema, asthmatic bronchitis, nasal polyps	Six weeks' duration only
3	Dyspnea, dizziness, thoracic pain	130	94		Negative	Sinus tachycardia, rate 100	Dyspnea, wheezing râles, heart enlarged	Emphysema, bronchitis, arteriosclerosis, obesity	Circulation competent
4	Dyspnea, dizziness, thoracic pain	108	70	3058 to 4522	Pneumokoniosis		Diffuse râles	Emphysema, pneumokoniosis, silicosis	Fibrosis of lung resulting in lowered vital capacity, 33.5 per cent of normal

5	Dyspnea, cough, dyspepsia	156	90	2911 to 4255		Rate 71, sinus rhythm, left ventricular preponderance	Heart and breath sounds distant, voluminous lungs	Emphysema, bronchitis, myocardial degeneration, coronary sclerosis	Years of respiratory and circulatory difficulty with gradual heart failure, no erythrocytosis
6	Dyspnea, cough	124	64		Bilateral pulmonary tuberculosis		Typical emphysema, barrel-shaped chest, dyspnea severe	Emphysema, chronic bronchitis, old tuberculosis	Very frail, very dyspneic, very low vital capacity
7	Dyspnea, hoarseness	130	70	4449 to 4000	Heart enlarged		Typical emphysema, dyspnea, marked cyanosis	Emphysema, chronic bronchitis, arteriosclerosis, coronary sclerosis	Heart enlarged but competent, question of polycythemia
8	Dyspnea, cough, profuse sputum, weakness	140	80	4648	Old lesion both upper lobes, pleural thickening		Dyspnea, cyanosis, râles in lungs, enlarged normal heart	Emphysema, mitral endocarditis	Compensated heart
9	Dyspnea, palpitation, asthma	152	80		Extensive fibrosis of both lungs		Râles throughout lungs, asthmatic breathing	Emphysema, asthma	Exophthalmic goiter, central aneurysm, or brain tumor
10	Dyspnea, cough, epigastric pain	120	90		Heart enlarged	Rate 75, sinus rhythm, right ventricular preponderance, P wave notched in leads II and III	Râles throughout lungs	Emphysema, asthmatic bronchitis, septic tonsils, inguinal hernia	Asthma ceased three years previously

11	Dyspnea, cough, sputum	110	80	1992 to 4572	Negative	Rate 81, sinus rhythm, right ventricular preponderance, QRS wave notched in leads II and III	Long narrow chest râles, no cyanosis	Emphysema, bronchitis, congenital pulmonary defect (?)	Dyspnea severe and produced invalidism, vital capacity reduced 57 per cent
12	Dyspnea, cough, sputum	108	80		Healed tuberculosis in upper lobe of right lung	Rate 109, sinus tachycardia, right ventricular preponderance, exaggerated P wave in lead III	Sibilant râles throughout, asthmatic breathing, heart sounds distant	Asthmatic bronchitis, nasal polyps, chronic nephritis	Polycythemia considered

TABLE 2
VOLUME OF BLOOD AND PLASMA IN CASES OF EMPHYSEMA AND ASTHMA

Case	Age	Sex	Weight, kg.	Ideal weight for height and age, kg.	Hemoglobin, gm. in each 100 c.c. of blood	Cells by the hematocrit, per cent	Erythrocytes, millions	Blood volume				Plasma volume		
								Total volume, c.c.	C.c. for each kg. of body weight	C.c. for each kg. of ideal body weight	C.c. for each square meter of body area	Total volume, c.c.	C.c. for each kg. of body weight	C.c. for each square meter of body weight
1	64	M	66	79	15.3	35		5890	89	75	3250	3830	58	2110
2	33	M	67	85	17.5	46	5.40	6170	92	73	3220	3330	50	1740
3	62	M	87	69	19.3	47	6.08	7150	82	104	3650	3790	44	1930
4	37	M	75	81	15.6	38	4.80	7080	94	87	3610	4390	59	2240
5	62	M	60	69	16.7	42	5.24	4930	82	71	2950	2860	48	1710
6	68	M	54	53	16.1	35	4.05	5570	103	105	3520	3620	67	2290
7	65	M	73	64	17.2	46	4.78	5950	82	93	3400	3330	46	1900
8	61	M	50	53	14.1	35	4.17	5020	100	94	3280	3260	65	2130
9	53	F	63	61	18.6	56	6.86	5340	85	88	3340	2350	37	1470
10	29	M	62	61	20.0	47	4.58	6040	99	99	3700	3200	51	1960
11	52	M	50	83	14.2	39	4.32	4920	98	59	3155	3000	60	1920
12	37	M	51	67	11.5	34	4.80	5150	92	77	3180	3400	66	2080
Mean value			64.1	68.7	16.5	42.5	5.02	5792	91.5	85.4	3367	3368	54.1	1960
Probable error			2.1	2.1	0.5	1.3	0.16	156	1.4	2.7	46	97	1.8	43.5
Normal values					15.6	42	5.00		87.7		3278		51.2	1920

oglobin in the cell for the group, was 40.9.

Erythrocytes in each cubic millimeter of blood—The number of erythrocytes for each cubic millimeter of blood varied from 4,050,000 to 6,860,000. The average count was 5,020,000. There were only two cases in which the erythrocyte counts reached 6,000,000, and seven in which they were less than 5,000,000 which is considered the normal erythrocyte count for each cubic millimeter.

Hematocrit values—The percentage of cells by the hematocrit varied from 34 to 56, with a mean of 42.5 which, according to the dry oxalate method, is normal. In five cases, however, hematocrit values were in excess of 45 per cent. This percentage is usually considered normal when the wet oxalate method is used.

TABLE 3

VOLUME OF CELLS AND CIRCULATING HEMOGLOBIN IN CASES OF CHRONIC EMPHYSEMA AND ASTHMA

Case	Total volume, c. c.	Cells		Circulating hemoglobin		
		C. c. for each kg. of body weight	C. c. for each sq. meter of body area	Total volume, c. c.	Gm. for each kg. of body weight	Gm. for each sq. meter of body area
1	2060	31	1140	903	13.6	499
2	2840	42	1480	1080	16.1	568
3	3360	38	1720	1380	15.9	705
4	2690	35	1370	1105	14.7	564
5	2070	34	1240	824	13.7	494
6	1950	36	1230	896	16.6	568
7	2620	36	1500	1025	14.1	586
8	1760	35	1105	708	14.1	463
9	2990	48	1870	994	15.8	621
10	2837	48	1740	1250	19.9	766
11	1920	38	1235	700	13.9	449
12	1750	34	1100	593	10.6	366
Average	2400	37.2	1394	954.7	14.9	554
Normal values		36.5	1358		14.7	541

Blood volume and plasma volume—The mean blood volume for the group of twelve patients was 91.5 c. c. for each kilogram of body weight (table 2 and 3). The range was from 82 to 103 c. c. Marked examples of obesity or of a condition of underweight were not present among the patients. The mean weight was 64.1 kg. If the ideal weight is calculated according to age, sex and height, a mean value of 68.7 kg. is obtained, which gives a mean blood volume for the group of 85.4 c. c. In the individual case, the calculation of the blood volume, according to ideal weight, does not indicate that there was a serious deviation in the blood volume except in case 3, in which 82 c. c. in each kilogram is changed to 104 c. c. On the basis of body area, there was a mean value of 3367 c. c. for each square meter, which is strictly normal.

TABLE 4

VOLUME AND HEMOGLOBIN CONTENT OF ERYTHROCYTES

Case	Volume index of the erythrocyte	Saturation index, hemoglobin	Volume of the average erythrocyte in c. c. x 10-11	Grams hemoglobin in average erythrocyte x 10-11	Actual percentage of hemoglobin in the erythrocyte
2	1.02	1.25	8.52	3.24	38
3	0.96	1.10	8.10	3.34	41
4	0.94	1.10	7.90	3.25	41
5	1.10	1.20	9.40	3.91	41
6	1.03	1.40	8.64	3.98	46
7	1.14	1.14	9.60	3.62	38
8	1.01	1.28	8.40	3.38	40
10	1.22	1.29	10.30	4.37	42
Average	1.05	1.22	8.86	3.64	40.9
Normal value (Haden)	1.00	1.00	9.20	3.12	33.9

The plasma volume varied from 37 to 67 c. c. and the mean value was 54.1 c. c. for each kilogram of body weight. The range for normal persons is from 48 to 60 c. c. In cases 3, 7 and 9, values were below the lower limit of normal. The cases with the higher plasma volumes were those in which there were mild degrees of anemia. The patient in case 9, with a plasma volume of 37 c. c. for each kilogram of body weight, was not obese, and the blood volume was 85 c. c. for each kilogram of body weight. This gives a cell volume of 48 c. c. for each kilogram of body weight as compared with the corresponding normal cell volume of 36.5 c. c. This represents relative erythrocytosis due to diminished plasma volume. If the plasma volume for the group is calculated according to the ideal weight, a mean value of 48.8 c. c. is obtained, a value slightly less than normal. According to body area, the plasma volume varied from 1470 to 2290, with a mean value of 1960 c. c. which is normal.

Oxygen content and saturation of blood—Studies of the oxygen content of the arterial and of the venous blood were carried out in seven cases of the group of twelve (tables 5 and 6). The blood was obtained by puncture of the radial or of the brachial artery and was collected under oil.

The oxygen content of arterial blood varied from 18 to 21.8 volumes per

TABLE 5

STUDIES OF OXYGEN IN THE ARTERIAL AND VENOUS BLOOD IN EMPHYSEMA

Case	Oxygen capacity, volumes per cent	Oxygen content				Utilization in the tissues	
		Arterial blood		Venous blood			
		Volumes, per cent	Percentage of saturation	Volumes, per cent	Percentage of saturation	Volumes, per cent	Percentage of saturation
1	20.5	18.3	89	10.6	51	7.7	37
2	23.5	20.6	87	16.1	68	4.5	19
3	25.9	21.8	84	14.9	57	6.9	26
4	21.0	19.2	91	8.0	38	11.2	53
5	22.4	20.9	93	5.0	22	15.8	70
6	21.6	18.0	83	6.5	30	11.5	53
7	23.0	20.7	89	17.5	75	3.2	13
Average	22.5	19.9	88.3	11.2	49.2	8.7	39.2
Normal values	21	20	95.6	14.5	70	5.5	26

cent, with an average value of 19.9. The oxygen capacity in volumes per cent averaged 22.5, which gave an average percentage oxygen saturation of the arterial blood of 88.3. This indicates a moderate grade of anoxemia; in no case was the percentage of oxygen saturation as high as normal. The lowest percentage of oxygen saturation was obtained in cases 3 and 6, 84.4 and 83.0 per cent, respectively.

The oxygen content of the venous blood varied from 5 to 17.5 volumes per cent, with an average value of 11.2 volumes per cent. The average percentage saturation was 49.2 which is an unsaturation approximately of 50 per cent.

The utilization of oxygen, which is the difference between the arterial and venous oxygen content, showed a wide variation, with an average value of 8.7 volumes per cent (normal 5.5 volumes per cent).

Studies of vital capacity—The vital capacity was reduced in cases 1, 2, 4 and 5. In case 7, it was equal to the normal estimated value.

TABLE 6
VOLUME OF BLOOD, PERCENTAGE SATURATION WITH OXYGEN OF ARTERIAL BLOOD AND VITAL CAPACITY

Case	Hemoglobin gm. in each 100 c.c. of blood	Erythrocytes, millions	Cells by hematocrit, per cent	Blood volume		Percentage saturation of oxygen of arterial blood	Vital capacity, c. c.	
				Total volume, c.c.	C.c. for each kg. of body weight		Actual volume	Estimated volume
1	15.3		35	5890	89	89	3128	4480
2	17.5	5.40	46	6170	92	87	3625	4735
3	19.3	6.08	47	7150	82	84		
4	15.6	4.80	38	7080	94	91	3058	4522
5	16.7	5.24	42	4930	82	93	2911	4255
6	16.1	4.05	35	5570	103	83		
7	17.2	4.78	46	5950	82	89	4449	4000
Average	16.8	5.06	41	6106	89	88.3	3434	4400
Normal values	15.6	5.00	42		87.7	95.6		

DISCUSSION OF SIGNIFICANT RESULTS IN GROUP 1

The hemoglobin content of the individual erythrocyte indicated 20 per cent more hemoglobin than is found by calculation, according to Haden, for the average normal erythrocyte.

The response of the blood in these twelve cases to the lowered saturation of oxygen was variable. One point is clear; that in no instance did the erythrocytosis develop to a degree to simulate true polycythemia vera. The volume of blood and cells, calculated on the basis of body weight, gave mean values for the group that were very slightly above the means for normal persons. Probably the difference is insignificant. In only two cases was the blood volume in excess of 100 c. c. for each kilogram of body weight. In one of these, anemia was believed to be present and the increase in blood volume is explained largely by the increase in plasma. In the second case, with a blood volume of 82 c. c. for each kilogram of actual weight, and of 104 c. c. for each kilogram of calculated ideal weight, the percentage of cells by the hematocrit and the concentration of erythrocytes were definitely high. This probably represents

an absolute increase of erythrocytes but not an increase to the degree observed in polycythemia vera. On the other hand, there was evidence of increased concentration of blood as determined by the percentage of cells by the hematocrit and by the number of erythrocytes in each cubic millimeter of blood; this was observed in cases 2, 3, 7, 9 and 10. In only one case (case 9) was this increase of significance, with 6,860,000 erythrocytes for each cubic millimeter of blood, and 56 per cent of cells by the hematocrit. In this case the volume of blood was normal with a diminished amount of plasma for each kilogram of body weight. This tendency to increased concentration without serious disturbance of the volume of the blood and cells for body weight or body area, explains the observations with reference to the individual erythrocyte as determined by calculation.

The studies of the oxygen content of venous blood have shown an unsaturation with oxygen of venous blood sufficient to produce cyanosis. Lundsgaard and Van Slyke have shown that unsaturation with oxygen to the amount of 6 to 7 volumes per cent in the capillary blood is necessary for cyanosis to be produced. The oxygen content of the capillary blood is not known, but probably is represented by the formula $\frac{A+V}{2}$, which is the mean between the degree of unsaturation with oxygen of the arterial blood and of the venous blood. When this formula was applied to the seven cases in table 5, cases 3, 4, 5 and 6 had unsaturation values sufficiently high to produce cyanosis. These criteria for cyanosis do not correlate well with the clinical evidence of cyanosis, but probably this discrepancy can be explained by modifying factors, such as the condition of the surface capillaries and pigmentation of the skin.

Arterial anoxemia determined in terms of percentage saturation, which is the ratio between the oxygen capacity and the oxygen content of the arterial blood, was present in all the cases in table 5. In all of these cases values were below the normal of 95 to 100 per cent saturation. In two cases (cases 3 and 6) low values of 83 and 84 per cent saturation were obtained.

The percentage reduction of vital capacity varied from approximately 33 to 50 per cent of normal.

The correlation of the volume of blood, vital capacity and percentage saturation of arterial blood is shown in table 6. Correlation was not demonstrable between the percentage saturation of arterial oxygen and the volume of blood and cells for each kilogram of body weight. In case 6, with the lowest saturation value, the highest blood volume was obtained, 103 c.c. for each kilogram of body weight, which if corrected for the ideal weight would be 105 c.c. and would constitute an example of slight increase in the volume of blood. This increase in blood was not due to an increase in cells but to an increase in plasma which probably was related to the mild anemia.

The data concerning the blood in cases of chronic pulmonary disease stimulate those obtained in experi-

mental work on the dog after evulsion of intercostal and phrenic nerves[8] which was followed by operative destruction of the respiratory function of the diaphragm. Studies on the blood were carried out months after the operation, and significant changes were not noted in the hematocrit or volume determinations. The arterial saturation was low (87 per cent) and the vital capacity was diminished. The results of all laboratory studies were similar to those in the clinical cases.

Comparison of Results in Group 1 With Results in Groups 2 and 3.

In contrast to the observations in chronic pulmonary disease, attention is called to those in the two cases in group 2, in which polycythemia vera was associated with chronic pulmonary disease (table 7). In these cases, the blood volume was enormously increased and the percentage saturation of oxygen in the arterial blood was markedly lowered.

The remaining case, which, by itself, constitutes group 3 is presented as a probable example of Ayerza's disease, in which the clinical picture is one of extreme cyanosis frequently associated with pulmonary emphysema, hypertrophy of the right side of the heart, marked dyspnea, and secondary sclerosis of the pulmonary artery. In this case, the oxygen saturation of the arterial blood was low, and the clinical data correspond well with those given as representative of the syndrome of Ayerza's disease. The blood volume was definitely increased to 114 c.c. for each kilogram of body weight. The spleen was not enlarged and there was no difficulty in excluding a diagnosis of polycythemia vera.*

The average hemoglobin in the individual cell is the cases in group 2 was 34 per cent and in the case of Ayerza's disease (group 3) it was 36 per cent.

Comment

It has been well established that there are large reserves of erythrocytes in the body that are not in active use in the circulation as oxygen carriers but that can be called into service by various stimulants. Emotional outbursts produce acute transient erythrocytosis. The result is obtained by calling all the available erythrocytes into the circulation and is a question of reserve of erythrocytes rather than of increase in production of erythrocytes.

When animals or man are subjected to a limited supply of oxygen, a similar response occurs. This condition exists at the high altitudes of mountain peaks, in airplane flights at great heights, and by artificial rarefaction at sea level. The effects are immediate and temporary; they persist only after long exposure to these influences.

The limitation of the supply of oxygen in the air may be simulated, in part at least, by conditions within the parenchyma of the lung that serve to decrease the available supply of oxygen to the blood. Patients with chronic pulmonary lesions, if anoxemia occurs, presumably should react in a similar way to that in which persons react who are subjected to long-con-

*This case has been reported as a complete study by Constam and Brown.

TABLE 7

VOLUME OF BLOOD AND OXYGEN SATURATION OF ARTERIAL BLOOD IN POLYCYTHEMIA VERA WITH CHRONIC PULMONARY OR CARDIAC DISEASE

Case	Age and Sex	Hemoglobin, gm. i 100 c. c. of blood	Erythrocytes, millions	Blood		Plasma		Percentage oxygen saturation of arterial blood	Comment
				C. c. for each kg. of body weight	Total volume, c. c.	C. c. for each kg. of body weight	Total volume, c. c.		
13	56 M	20.7	6.34	168	6360	67	2540	78.0	Polycythemia vera, splenomegaly graded 2, chronic bronchitis, emphysema, cyanosis graded 3
14	43 M	25.6	7.67	185	6150	52	1720	69.5	Polycythemia vera, splenomegaly graded 1, chronic emphysema, myocardial insufficiency, cyanosis graded 3
15	27 F	16.9	4.52	114	7300	59	3790	74.8	Ayerza's disease, emphysema, cyanosis

tinued residence in places where the air is rarefied.

With these premises, it seems legitimate to expect that, although external respiration may be faulty, either because of anatomic defect or in consequence of limitation in the supply of oxygen, the requirements of internal respiration may be satisfied by an increase in oxygen carrying power.

Laboratory and experimental results give ground for statements of general facts which often are not applicable to the complicated conditions present in the illnesses of man. Chronic emphysema, usually complicated by bronchitis, provides a suitable subject for study in this connection. Patients afflicted with this disease are ambulatory, well past middle life, dyspneic on exertion, and frequently when at rest also; they are cyanotic under similar circumstances and have hearts in which degenerative changes are to be expected as the rule rather than as the exception. The pathologic changes within the lung are progressive and unlimited in degree, so that the effort at compensation is long continued, and ultimately fails. The right side of the heart loses competency just as the left side also may lose competency in conditions in which hypertension is produced.

The thin and ruptured alveolar walls, the broken elastica, and the constricted capillaries are characteristic of the disease, and when emphysema is marked, the flow of blood in the lungs is impaired and the patient is comparable to one living for a long period of time at high altitudes with respiratory embarrassment and increased pressure of the pulmonary circulation. The right side of the heart hypertrophies, then dilates, and dyspnea is followed by cyanosis.

Summary

In cases of chronic pulmonary disease, chronic emphysema and bronchitis, the response of the blood to arterial anoxemia was variable. Increases in the volume of blood and cells never simulated those found in polycythemia vera. When erythrocytosis was observed, it seemed to be due to changes in concentration, and in only one case was erythrocytosis present to a striking degree. There was an increase in the amount of hemoglobin in the individual erythrocyte. Correlation was not demonstrated between the vital capacity and the degree of arterial anoxemia, or the vital capacity and the response of the blood. Likewise, correlation could not be demonstrated between the arterial anoxemia and the response of the blood. The vital capacity was reduced in some instances to a very significant degree. Cases of polycythemia vera, complicated by pulmonary disease and marked unsaturation with oxygen of the arterial blood, showed the usual excesses in the volume of the blood and cells that are observed in uncomplicated cases of polycythemia vera. In one case of Ayerza's disease there was demonstrated erythrocytosis of sufficient degree to produce significant absolute increases in the volume of the blood and cells.

The clinical observations and the data obtained in this study demonstrate the degree of dysfunction that may take place in respiration before normal reserve is overcome and the collateral function of circulation is called on for compensatory assistance.

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The Treatment of Neurosyphilis*

By H. C. Solomon, M.D., *Boston, Mass.*

1. It is now possible to obtain an apparent arrest in all forms of neurosyphilis.

2. Not all cases of any form or variety of neurosyphilis can be arrested.

3. Febrile methods and tryparsamide are the most effective means available in the treatment of neurosyphilis. Intraventricular, intracistern, intraspinal serum injections, as well as arsphenamin, bismuth, mercury, and iodid, are of secondary importance.

4. The arrest of late and advanced and malignant types of neurosyphilis give strong evidence that when cases are treated earlier they can be arrested before great damage has occurred.

5. Improvement in our methods of treatment is to be hoped for and expected.

By "apparent arrest" of the syphilitic process in cases of neurosyphilis is meant that there is a complete serological recovery and a cessation of the progress of the clinical symptoms. This has been achieved in practically all types of neurosyphilis including the meningo-vascular forms, tabes, and paresis. There is insufficient pathological data available at the moment to insist that the activity in the cases of general paresis is entirely halted. However, there is being accumulated a considerable amount of evidence which leads to the belief that a true arrest is obtained. It will suffice for the present discussion, however, to talk of apparent arrest until such time as one has more convincing evidence.

For many decades it has been known that cases of the meningo-vascular varieties of neurosyphilis could be arrested and apparently cured by the use of mercury and iodid. Later, with the use of arsphenamin, an increasing percentage of these cases, whether in the early or late stages, were found to recover with the use of this drug. Whereas, tabes did not give satisfactory results when treated with mercury, arsphenamin produced quite satisfactory clinical and serological results in a small percentage of cases. Serum injections into the subarachnoid space added greatly to the number of cases both of the meningo-vascular and tabetic varieties of neurosyphilis which reacted well. The fact that serological recovery and clinical improvement could be obtained, gave proof that these cases were of the type that could be successfully treated. The problem narrowed down then to a matter of getting a higher percentage of good results.

*Read before the Boston Meeting of the American College of Physicians, April 10, 1920.

In cases of general paresis, the problem of treatment presented itself in clearer form. Mercury and the iodids, according to all experience, produced no satisfactory results whatsoever. Arsphenamin, in ordinary dosages, was practically no more effective. Very large doses, often repeated, appeared to give improvement in a small percentage of the cases, but by no means was it conclusively proven that it caused a definite arrest or serological cure in any but rather exceptional cases, nor did intraspinal or intracisternal injections of arsphenaminized serum give conclusive evidence of arrest. Cases of paresis, therefore, offer the ideal material for the evaluation of other methods than those mentioned.

Malaria, as the prototype of febrile therapy, has been used and the results studied for the past ten years. Tryparsamide, a pentavalent arsenical preparation, has been used and the results studied for approximately six years. While these periods are too short to draw any definite and final conclusions, they are long enough to have given us an opportunity to gather a considerable amount of evidence concerning their effectiveness in the treatment of general paresis, and other types of neurosyphilis as well. A conservative summary of the literature of the world concerning the results obtained with malarial treatment indicates that a thoroughly good clinical result is obtainable in about 30% of the cases of general paresis, while approximately another 30% show a reasonable amount of improvement. Complete tabulation of the results obtained in the treatment of paretic cases by tryparsamide is not available, but what information is at hand would indicate that results are substantially the same as obtained by the use of malaria. The important factor to be stressed is that with both these methods, it is possible to obtain complete serological recovery in a considerable number of cases.

The point of serological recovery is extremely important, to my way of thinking. While natural remissions occur occasionally in general paresis, I have seen no evidence to indicate that serological improvement, much less complete serological recovery, occurs spontaneously except possibly in a rare instance where an intercurrent infectious disease has produced febrile effects similar to what are obtained artificially by malaria. In other words, a serological recovery is evidence that the method of treatment used has been effective in producing results which cannot be considered as accidental or coincidental. Wagner von Jauregg, the introducer of the febrile method, and his co-workers, at first laid down the dictum that serological modification was unimportant because cases which showed a degree of serological improvement at times made no definite clinical improvement, and on the contrary, cases showing excellent clinical remissions did not show parallel improvement in the serology. Later studies have, I believe, modified this point of view very materially. Cases that do not show serological improvement are the ones that are most likely to relapse, whereas, the cases which have both clinical and serological recovery are the ones most likely to remain stationary and without relapses.

With malarial treatment serological improvement is quite slow in making

its appearance. In fact, only a slight improvement is usually seen within six months after treatment, and it is not until twelve to twenty-four months that the maximum amount of serological improvement is discernible. However, for this discussion I lay great stress upon the point that many cases have now been observed in which, following malarial treatment, a completely normal cerebrospinal fluid has been obtained.

Tryparsamide appears to affect the spinal fluid in a favorable fashion somewhat more frequently and somewhat more rapidly than does malaria. In neither case is it possible to offer satisfactory percentage figures, and one will have to be satisfied with such a statement, as just made, as the best conclusion that can be drawn without substantiating figures. My personal experience has been that it is possible to get a completely negative spinal fluid in a considerable percentage of the cases of general paresis, even including the quite far-advanced cases. In dealing with a group of institutionalized paretics who have been in a hospital for one, two, or three years before treatment was instituted, we have been able in more than 50% of the cases to get a practically negative spinal fluid. Most of this group of cases were quite deteriorated mentally and showed little, if any, mental improvement. Physically, improvement occurred and, most important, the disease did not seem to progress, the mental condition remained stationary, and the patients have lived for a longer period than would be the ordinary expectancy in such cases untreated.

These facts seem to me to offer definite proof that cases of the most malignant type of neurosyphilis can be arrested or, at any rate, so nearly arrested than no obvious progress of the disease process takes place in the course of several years. I do not believe that it is possible to draw any valid conclusions as to the comparative efficiency of these two methods. They both give relatively satisfactory results in a percentage of the cases, a percentage which is far from reaching 100. Both have certain advantages and disadvantages. The febrile method often works more rapidly, as far as clinical improvement is concerned, than does tryparsamide. At times it apparently fails when tryparsamide succeeds. Febrile treatment is a type of treatment that is fraught with danger, and a small mortality is to be expected through its use. Likewise, it is not available for patients in bad physical condition. The delay in improvement which may be found in the use of tryparsamide, may at times be a definite contra-indication. Tryparsamide will occasionally cause amblyopia, and in certain cases, therefore, will not be available. Malaria treatment at times causes arrest in cases that are not doing well with tryparsamide.

It must be emphasized that in the treatment of established cases of general paresis, neither method gives anywhere nearly as high a percentage of satisfactory results as one desires. It is my personal belief that very often the combination of malaria and tryparsamide will achieve a good result when either alone does not accomplish this. This is a point on which there is a difference of opinion, but personal experience has thoroughly convinced

me of the validity of this belief. It is not possible at this time to go into the details of method. I would only state that at times we use several attacks of malaria, as well as other methods of producing fever, with a very long course of tryparsamide aided by arsphenamin and mercury, bismuth, iodids, and at times subarachnoid injections.

Accepting the statement as correct that cases of the most malignant form of neurosyphilis, namely, the paretic, can be arrested, it would seem to follow that the less malignant forms should give us a much higher percentage of success, and this seems to be the case. A very high percent indeed of cases of tabes may be arrested by tryparsamide alone or tryparsamide in conjunction with arsphenamin and intraspinal injections. In the simpler forms of meningeal and meningo-vascular neurosyphilis, the percentage of success now approaches 100%. Of course this does not mean that the degenerative changes can be completely halted nor that sclerotic changes in the blood vessels will be stopped from progressing.

I hope I have made clear that valuable as I consider tryparsamide and malaria and other febrile methods in the treatment of paresis and neurosyphilis, I do not consider them by any means adequate for the treatment of malignant late cases. There are two solutions to be hoped for. First, that we can obtain more efficient methods. Tryparsamide and febrile methods are only indications of the possibility of improvement in the ways and means of treating these cases, and we have every reason to suppose that in the future more valuable means will be made available.

The second possibility of improving the situation very markedly is the early recognition of central nervous system involvement. The degree of success which we now have with the late and malignant forms of the disorders is evidence that earlier diagnosis followed by our now available methods of treatment will arrest the disease before appreciable damage to the cord or brain has occurred. In the asymptomatic forms of neurosyphilis, the forerunners of clinical meningo-vascular, tabetic, and paretic neurosyphilis, the serological recovery is to be expected in nearly every case. It is only a matter of early recognition and continuation of treatment for a sufficient length of time, then the application of the method which is efficient for the given case. In almost all of the asymptomatic cases, and certainly in the majority of the cases of meningo-vascular and tabetic forms, the febrile method is not necessary. Combinations of tryparsamide, arsphenamin, mercury and bismuth and intrathecal injections will practically always succeed.

Finally, I would call attention to the long-continued treatment that is many times required to produce a serological recovery. It is our usual custom when using tryparsamide to continue it indefinitely and usually without interruption until the desired result is at hand. Having sufficient optimism to believe that a serological recovery is nearly always available, we persevere, however long it may take, week after week, month after month, and year after

year. The highest number of tryparsamide injections which we have given to any one patient up to now is 183 injections in a period of little less than five years. There is rarely any evidence of cumulative effects or lack of ability of patients to handle the drug. Our present working motto is that a serological arrest, at any rate, is to be expected in practically every case with the methods now available, and it is our problem to use the methods to the best advantage and to continue them until the desired result is obtained.

Syphilis of the Lung*

By Robert I. Rizer, *Minneapolis, Minn.*

I HAVE chosen to speak to you to-night about syphilis of the lung because it is a rare disease, it is difficult to diagnose, and for the first time in my twenty years of practice a case has come under my personal observation.

On January 20, 1928, a single American woman, aged forty-five years, came to our office complaining of a constant dull ache in her right chest. This had been present for several months without remission. It had never been sharp or severe. With the movement of her body and arms the distress increased. She was unusually tired and required more rest than ever before. She had lost from seven to eight pounds in six months, but had had no fever, chills, cough, expectoration, or other symptoms.

This patient had been well until the fall of 1913. At this time she first noted a pain in the chest area. The pain was constant and bothered her to such a degree that she stopped work for a few days and called a doctor, who strapped her chest. At that time, she had no cold, fever, chills, sweats, or expectoration. It was thought that she might have tuberculosis. However, no X-ray examination was made. After a few days rest, she returned to work, with no symptoms. The distress recurred at intervals during the winter, and when it became very severe the doctor again strapped her chest. This gave her immediate relief. She had no fever at any time. After the spring of 1914 she had only an occasional "stitch in her side," but these were not distressing enough for her to see a doctor.

In the spring of 1927 while traveling in Europe, she developed an acute cold. The doctor said that she had a bronchitis and put her to bed. The pain returned, the same in character as before. She had a temperature of 101° to 102°, and a dry cough without expectoration. She remained in bed about one week, and at the end of twelve days resumed her journey, feeling well. No X-rays were taken. The patient's condition was good until the fall of 1927, when she stopped work for a few days because of the return of the same old pain. At this time an X-ray examination of her chest was made. This showed an infiltration into the right lung, and because there was no fever, chills, cough, or expectoration, her doctor felt that she had an acute respiratory infection. Her pain continued, and she saw me in January, 1928.

In this case family and past history are entirely negative. Physical examination shows her to be well developed and well nourished. Eyes react nor-

*Read at the Boston meeting of the American College of Physicians, April 9, 1929.

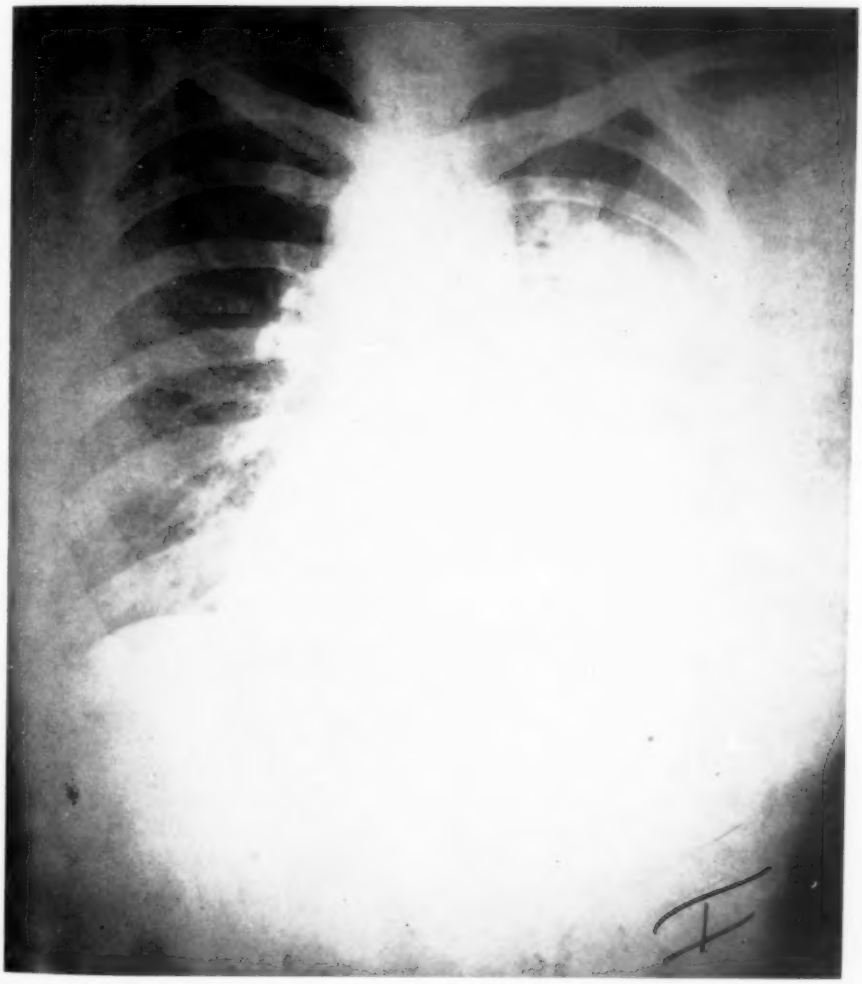

FIG. 1. Original plate of chest showing the syphilitic infiltration into the right, middle, and lower lobes (before treatment).

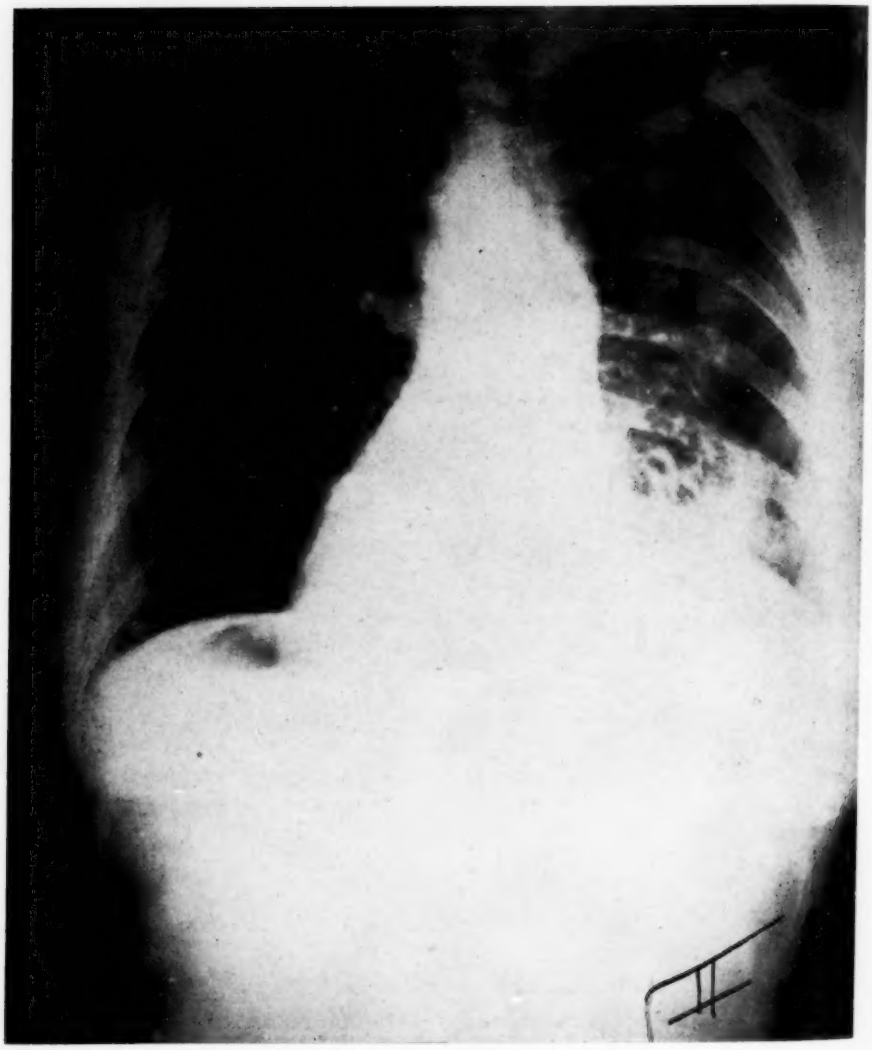

FIG. 2. Same after four weeks of active treatment.

mally to light and distance, sclera is normal. The nose is normal. The teeth are in good condition. The tonsils are slightly submerged, but nothing can be expressed from them. The thyroid gland is normal. No masses can be felt. Small glands are palpable in the neck, axilla, and groin. The breasts are normal. The chest is normal in shape. The right side of the chest has a slightly increased dulness at the base anteriorly. The breath sounds are suppressed, no râles are heard. The heart is normal in size, shape, and position. The rate is 85, and the rhythm is normal. Blood pressure is 110/75. The liver and the spleen are not palpable. The extremities and the reflexes are all normal. Abdominal, pelvic, and general sensory examinations are negative. Laboratory data: Urine, negative. Gastric content shows no free hydrochloric acid, microscopic negative. General blood examination, R.B.C. 4,260,000, W.B.C. 7,200, hemoglobin 81%, differential, Pmns. 45%, S.L. 28%, L.L. 10%, L.M. 1%, Tr. 2%, Eos. 4%, no abnormal cells seen. Blood metabolics, blood sugar .078%, urea nitrogen 11.3 m.g. Four stools negative. Kahn four plus, Wasserman four plus. We were unable to obtain sputum for examination. Electrocardiogram was normal. Because of the findings in the chest and the report from the X-ray examination, a bronchoscopic examination was made and found to be normal. The X-ray examination shows a hard, nodular, homogeneous type of consolidation extending out from the root of the right lung into the right middle and lower lobes, presenting a sharp line of demarcation from the normal lung. There did not seem to be anything in these films characteristic of a disease that we had ever seen. In comparing these films with those previously taken, we were at once aware that we were dealing with a progressive disease. Because the infiltration had extended, the roentgenologist felt that the most probable condition which this film represented was a Hodgkins disease. Clinically we found no evidence of this disease.

On the following day the Wasserman reports were returned four plus. With this report at hand, we wondered whether or not this might be syphilis of the lung. On consulting with a number of our colleagues we were as much confused as before, because no one consulted had seen a case of pulmonary syphilis, and no one was able to identify the film as such.

We were all agreed that if the patient with a chronic, progressive lung disease showed a marked improvement clinically and by X-ray examination under active treatment for four weeks, we would be justified in making a diagnosis of pulmonary syphilis. The patient was placed under active antisyphilitic treatment, and at the end of four weeks she showed great improvement clinically, and X-ray examination showed the infiltrated area to be much smaller. We then made a positive diagnosis of syphilis of the lung, and continued treatment. At the present time the patient has no symptoms. X-ray examination shows the chest to be practically normal.

In the medical literature there are probably between two and three hundred authentic cases of pulmonary syphilis. This is interesting in view

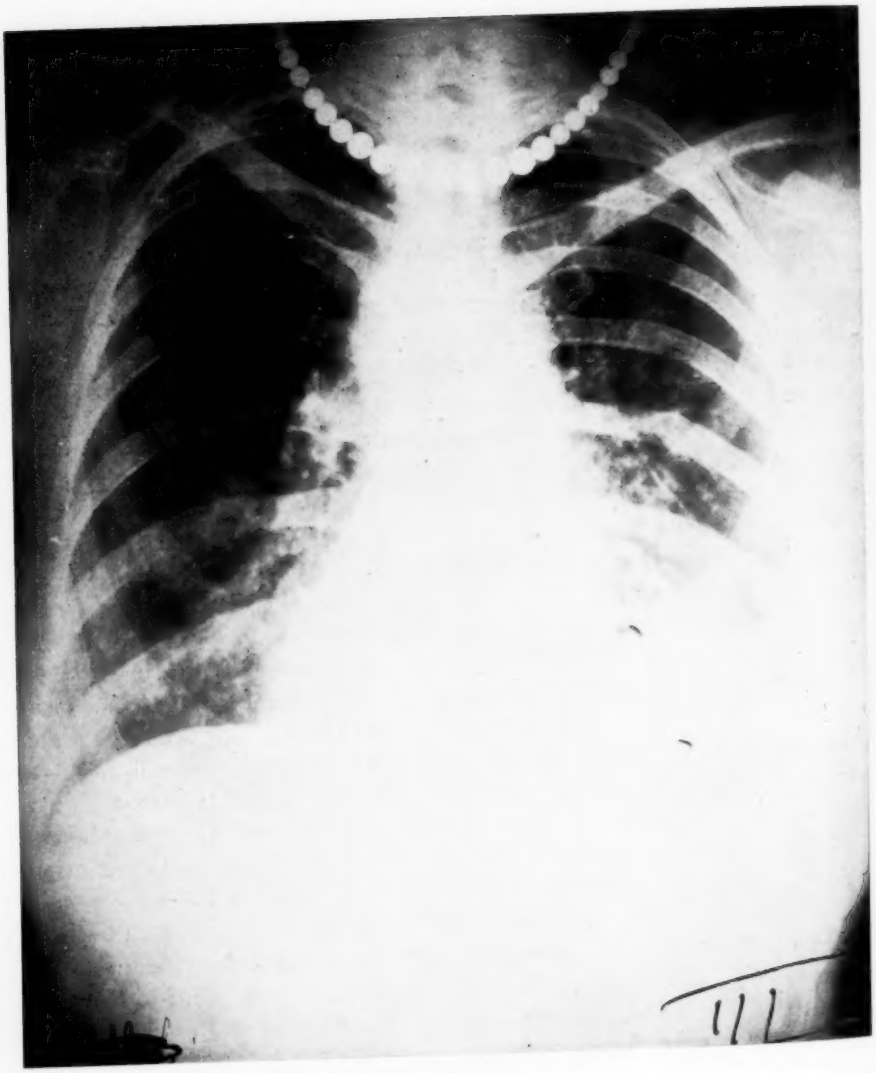

FIG. 3. Same after six months.

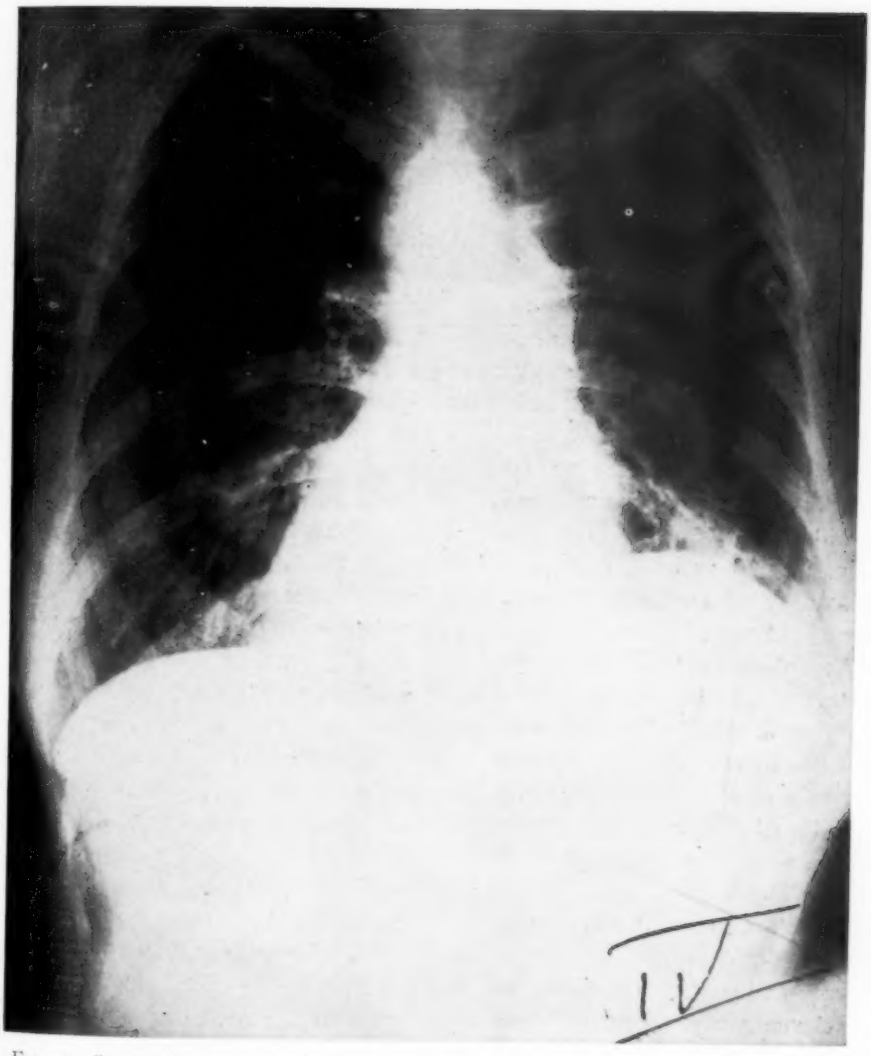

FIG. 4. Same after one year's treatment showing almost complete disappearance of the syphilitic infiltration.

of the fact that about three per cent of the entire adult population is syphilitic.

In 2800 autopsies at Johns Hopkins Hospital, twelve cases of lung syphilis were found. In 4480 autopsies in New York, there were twelve. In 5456 autopsies in California, there were twenty-nine. Fifty per cent of five hundred cases of pulmonary disease in Texas were syphilitic. In Michigan, 7.8% of 152 bodies showed lung syphilis. In 1300 specimens at the Army Medical Museum no syphilis was found. In the London Pathological museums, twelve. In England, among 100 cases reported to be tuberculous, two were definitely syphilitic. In South Africa, where tuberculosis is rare and syphilis common, 35% of all the natives had a fibroid condition of the lung. In Arizona, in 948 patients with advanced pulmonary tuberculosis, 28% showed x-ray evidence of pulmonary syphilis.

According to Dieulafoy, syphilitic lesions of the lungs are never early. They are probably later than syphilis of any of the other viscera. Save for exceptional cases, it may be said that syphilis of the lung appears only in the advanced tertiary stage of the disease. The interval between the primary infection and the development of the lung lesion varies between one and twenty-five years. The average is ten to eleven years. The ratio of lung syphilis to visceral syphilis is roughly one to twenty.

Karsner states that there is no definite picture of pulmonary syphilis. However, many observers state that the presence of plasma cells particularly about the blood vessels and bronchi, are characteristic of lung syphilis. The finding of spirochetes is unusual. Our Dr. Warthin is outstanding in that he is one of the few who has demonstrated their presence in the lung tissues.

Chesney has shown in his experimental work in rabbits how fibrous tissue favors the growth and development of spirochetes.

The pathology of pulmonary syphilis is similar to that of pulmonary tuberculosis. The acute and the chronic types of the disease are found. In the chronic type, miliary gummata may be present and increase in size and number until consolidation exists. Organization may occur or progress to softening with abscess, cavity formation, gangrene, or fistula, rarely to calcification. Fatal hemorrhages may occur. Regeneration of connective tissue may be present, especially about the bronchi and the vessels, or be massed, producing a lung cirrhosis with great deformity and possibly bronchiectasis and pleurisy. Large single gummata are rarely found. Microscopically mononuclear leucocytes and plasma cells are said to be frequently found in syphilitic scar tissue. Syphilis of the vessels of the brain and the aorta, testicles, bone, skin, and amyloid changes are most frequently associated with lung syphilis. Pulmonary tuberculosis is associated in from 3% to 11% of the cases of pulmonary syphilis.

The acute form with a sudden onset of fever, weakness, cough, with or without expectoration, dyspnea, weakness, and sweats, has been described, but it is not common. The chronic form of pulmonary syphilis with a slow, insidious onset, in course re-

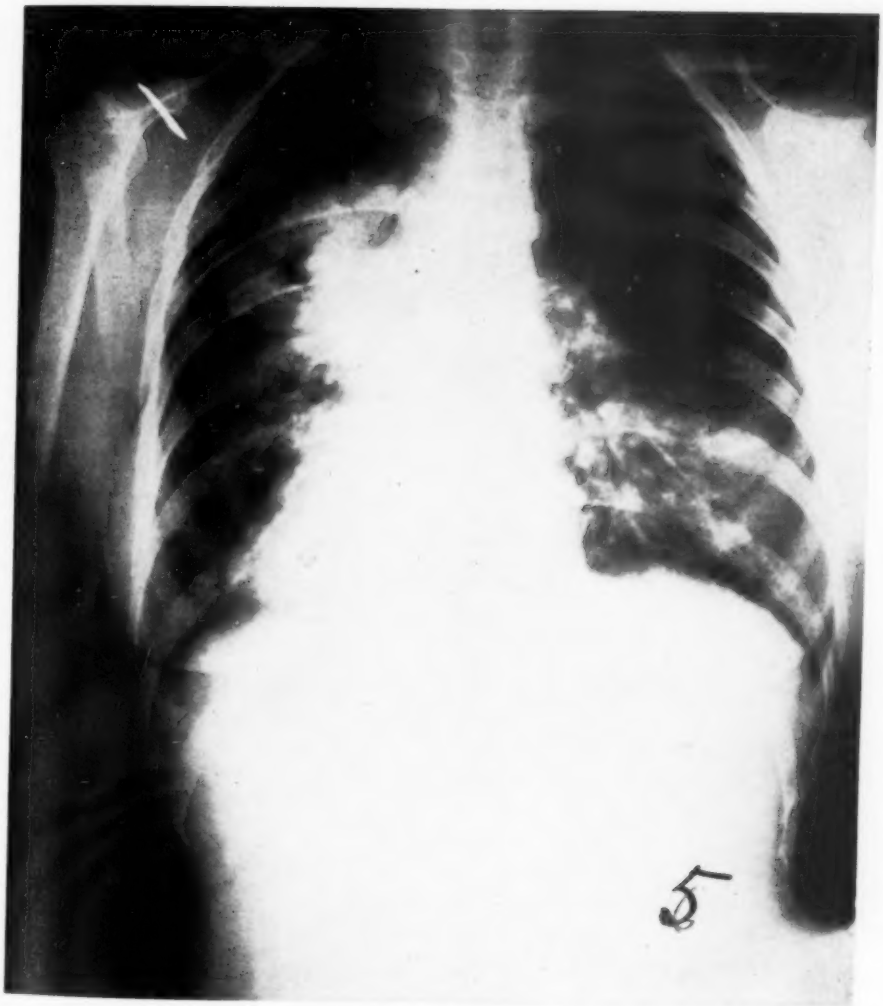

FIG. 5. Hodgkins Disease. Original plate of chest showing Hodgkins infiltration into left lung.

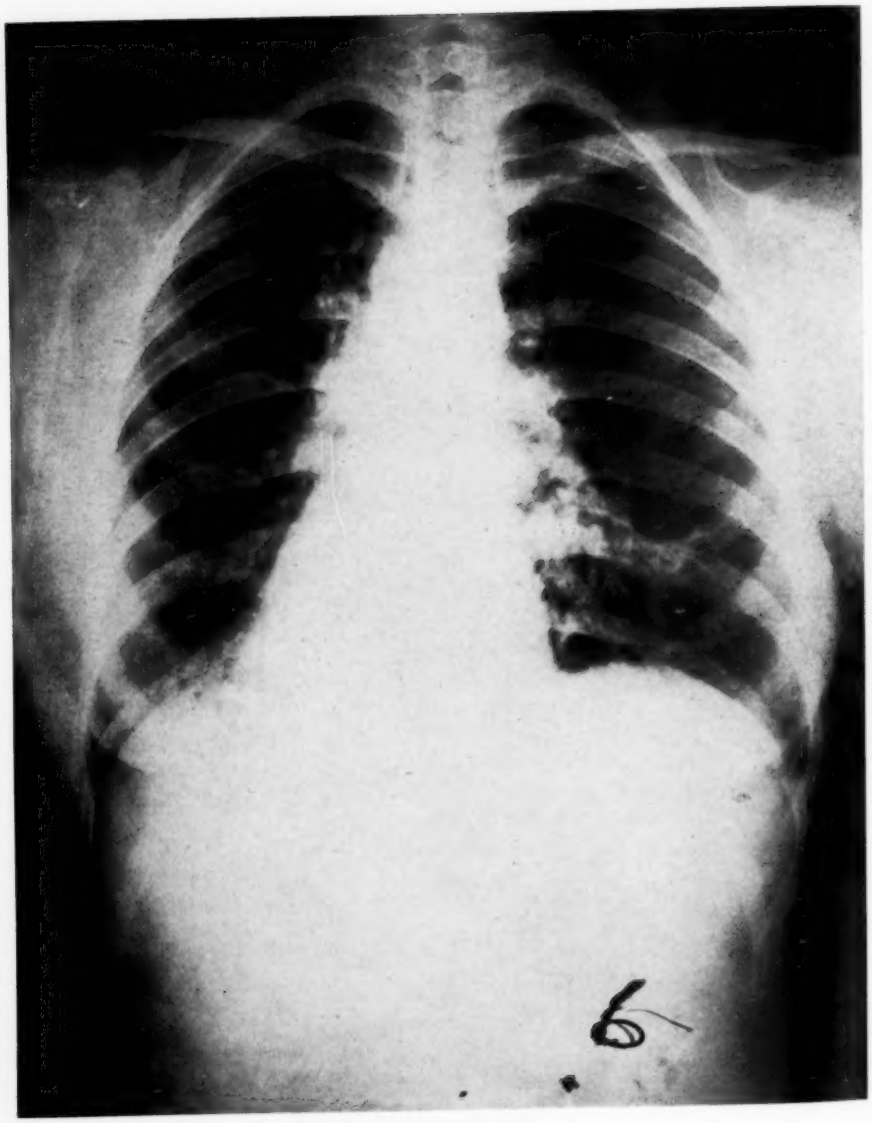

FIG. 6. Same as Figure 5 after X-ray treatment.

sembling a chronic tuberculosis, having very little fever, weakness, loss of weight, cachexia, and dyspnea out of proportion to the physical findings is similar to our case, and the form most commonly met with in medical practice. The chronic forms with softening, abscess, and gangrene, are like the tuberculous varieties. The bronchiectatic type is not different from any bronchiectatic disease. The physical signs simulate those found in pulmonary tuberculosis, varying according to the existing pathology. The spirochete has not been found in the sputum. The Wasserman is positive in more than fifty per cent of the cases. X-rays usually show a unilateral infiltration involving the middle and lower lobes, beginning near the hilus and extending peripherally.

An individual complaining of symptoms referable to the chest with dyspnea, in whom the physical and X-ray examinations of the onset show a unilateral lower lobe lung disease, a positive Wasserman, with or without other forms of syphilis, and a negative sputum should be diagnosed as having a pulmonary syphilis. Tuberculosis, sporotrichosis, aspergillosis, blastomycosis, pulmonary distomatosis, cysts, tumors, and Hodgkins disease should be considered in making a diagnosis. The prognosis of early lung syphilis is good unless the syphilis of some other part, as the brain or vessels (aneurism) is too far advanced. Then the prognosis is not good. The usual vigorous anti-luetic treatment should be used with frequent physical, blood, urine, and X-ray examinations.

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The Need for Emotional Data in the Medical History*

By John Favill, A.B., M.D., F.A.C.P., *Chicago, Illinois*

THIS paper is a neurologic plea to internists to make, as a routine proceedure in all medical histories except those of acute infections, some definite inquiry about possible disturbing emotional factors. By the latter I of course do not mean so-called unconscious matters which belong to the orthodox psychoanalyst. Neither do I suggest any intensive "third degree" probing by a junior intern who takes histories. But I am certain that many cases could be saved much delay and expense were the opportunity offered them early to state the existence of painful memories, present dilemmas or fears regarding the future.

Two conditions are necessary for the obtaining of such data. First, the patient must be convinced that it is relevant and may be important; second, the patient must be impressed with the truthworthiness of the questioner and the institution he may represent. It is obvious that these conditions cannot always be fulfilled. An attempt to meet them, however, would certainly yield more results than the lack of any such attempt, and even a failure would prevent a given functional patient from subsequently criticizing the doctor or the hospital for never having asked about what later proved to be the chief source of difficulties.

This is not the place and I am not the person to prove any theory of the emotions. But I will state a practical viewpoint for human beings with some simple examples. I think of awareness as a mystery which each of us carries and which I cannot explain. In it appears a sensation such as pain due to a nerve impulse initiated by an external pin. A thought follows: "It is a pin in the back of the chair." So far there is little if any emotion. But, on turning around, an unruly child is seen grinning with a pin in hand. A new thought comes: "That child ought to be spanked." This starts anger. Or, again, a sensation of pain appears as the result of an internal wave of peristalsis. The first thought, "It is those baked beans I ate for lunch," causes no particular emotion. But remembering a recently read medical article brings the thought "It is the lower right side and may be acute appendicitis." This easily lights a fire of fear. Finally, a person expectorates something bloody into a wash bowl. If he has had a tooth extracted an hour be-

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fore, there is no emotional disturbance. If, however, he has had no obvious cause for it but has been having bronchitis for months and the expectoration followed a cough, then the quick stream of ideas of tuberculosis, Arizona, interrupted career and death produce almost instantly an emotional state which may be acute.

Thus emotion appears to be a result of certain thoughts, somewhat as a sensation is the result of certain stimuli. The thoughts need not be in any language, they may be visual or other images with concepts of relationship or causality or potentiality, but I feel sure that some such awareness of a situation must precede the phenomenon we call emotion.

What follows the emotion is an individual affair. Effects will sometimes show in the endocrine, sometimes in the vegetative, sometimes in the voluntary motor system. I cannot consider these effects as part of the emotion itself.

Such effects are, however, undeniably the cause of many and various symptoms. Prominent among them are: pallor, blushing, pylorospasm, cardiospasm, vomiting, diarrhea, syncope, precordial pain, palpitation, sweating, polyuria, tremor, dry mouth, dilatation of the pupils, and sense of impending death. These symptoms are often the causes of new emotional disturbances. A vicious circle results. A simple example of this sort is illustrated by the following case.

T. C., male, aged 27, married, was seen December 19, 1928, complaining of slight pain in the top of his head, a sensation of something coming up from the stomach, and sweating hands. These symptoms had been occasionally present for several years, but now were coming in short attacks occurring many times a day. He feared death during most of them, and felt unable to continue his work as a clerk. He stated that he had been to at least seventy-five doctors, most of whom had examined his heart at his request and found nothing wrong. On inquiry, I found his first attack had occurred four years previously when he was hanging by both hands onto the rear of a crowded street car. He feared he would fall off but did not. The second attack occurred one year later and in it he noticed palpitation. (His position in the first attack would have prevented his noting this.) Other attacks came with gradually increasing frequency. He admitted that fear of death was the worst feature of the attacks. It was explained to him that the first one might have been a palpitation from some unimportant cause but which became the starting point for a severe fear reaction. Search for causes of palpitation revealed no organic disease but there was a history of excessive coitus, excessive tobacco chewing and cigarette smoking, at least four cups of coffee daily and the habit of bolting his meals whether hurried or not. He accepted the explanation after some hesitation and agreed to change his habits. He stated that not a single one of the seventy-five physicians previously consulted had made any inquiry along these lines or any similar suggestions. He has continued to work and not returned for further treatment.

In my experience a very distinct majority of cases having this general

type of disturbance have not buried the data in the unconscious. At least sufficient data is available in the majority to permit a procedure leading to a satisfactory adjustment. This procedure includes: first, correcting erroneous beliefs about symptoms, diseases, etc.; second, bringing to the patient an understanding of the chain of events; and third, encouraging him to form new reaction habits. Among the factors determining the result, on the part of the patient, are constitutional defect, age, severity of disturbing factors, intelligence and cooperation. On the part of the physician there is need for intelligence, unfailing patience, and sincerity.

The neuropsychiatric brotherhood has appreciated the importance of these matters for many years. The body of internists seems often to have been either impatient or neglectful or ignorant of them. It is only two years since the chairman of the section on medicine of the American Medical Association gave as his address "Psychic and Emotional Factors in General Diagnosis and Treatment,"[1] which was followed in the same session by a series of papers on phases of this problem. I have looked through a number of books and manuals on history taking and found little of what I want to propose. "The Clinical History in Outline"[2] gives a single line, "Psychic disturbances: shock, worry grief." "The Examination of Patients"[3] makes no definite suggestion. "History Taking and Recording,"[4] does refer the user to Kirby's[5] excellent manual, but in itself gives only the words "Emotional State" in two places. A more satisfactory suggestion occurs in Dock's "Outlines for Case Taking,"[6] consisting of this list: repressed desires, moral or physical shock, business cares, over-exertion, fright. This occurs, however, only in the section for diseases of the nervous system.

For some years I have been using a certain skeleton framework for history taking and the teaching of it which has the advantage of lessening the burden on memory and of presenting a complete scheme of arrangement of data. A mere glance at it often suggests lines of inquiry which otherwise would be forgotten and the place of each item is made obvious. (See Fig. 1.)

The division by systems, usually limited to the physical examination if used at all, is here carried back through the complaint and forward through the end result. The letters across the top refer to Complaint, Present Illness, Past History, Habits, Family History, Examination, Laboratory, Diagnosis, Treatment and End-result. The systems at the left are self-explanatory except for the fifth which means "Blood, Lymph, Endocrine and Unclassified." The numbers are merely

[1]R. T. Woodyatt. Jour. A. M. A., Vol. 89, No. 13, Sept. 24, 1927, P. 1013.

[2]P. G. Wooley. C. V. Mosby Co., St. Louis, 1916, P. 29.

[3]Nellis B. Foster. W. B. Saunders Co., Philadelphia and London, 1924.

[4]James A. Corscaden. Paul B. Hoeber, New York, 1926, PP. 28 and 52.

[5]Geo. H. Kirby. "Guides for History Taking and Clinical Examination of Psychiatric Cases." N. Y. State Hospital Commission, Albany, 1921.

[6]George Dock. Geo. Wahr. Ann Arbor, Mich., 1921, P. 34.

SYSTEM	C	PI	PH	H	FH	E	L	D	T	RES
Circulatory	1	11	21	31	41	51	61	71	81	91
Respiratory	2	12	22	32	42	52	62	72	82	92
Alimentary	3	13	23	33	43	53	63	73	83	93
Urinary	4	14	24	34	44	54	64	74	84	94
B.L.E. etc.	5	15	25	35	45	55	65	75	85	95
Reproductive	6	16	26	36	46	56	66	76	86	96
Skeletal	7	17	27	37	47	57	67	77	87	97
Tegumentary	8	18	28	38	48	58	68	78	88	98
Nervous	9	19	29	39	49	59	69	79	89	99
Mental	10	20	30	40	50	60	70	80	90	100

Fig. 1. Chart showing 100 possible divisions of a complete systemic medical history record.

for paragraphing purposes. Even they are easily remembered since in a given system, such as Alimentary, they always end in the same digit, 3-13-23 etc. A given part of the history, such as Habits, is covered by one decade, 31-32-33 etc. to 40. The lists of items possible for recording or inquiry under each number are quite debatable but I have worked out what I believe is a fairly satisfactory series of lists which I hope to offer for consideration at a future date. It must not be thought that I expect such a framework to be often completely fulfilled. Its use however as a reference system for thinking I believe is well justified.

The present suggested inquiry falls under paragraphs 10-20-30-40-50. This means Complaint, Present Illness, Past History, Habits and Family History—all in regard to mental items, somewhat as follows:

Par. 10. Complaint, if not forthcoming, may be covered by a simple question such as "Have you noticed anything different recently with your memory, thinking power, concentration or emotional balance?"

Par. 20. Present illness, if any, will be taken practically in patient's words.

Par. 30. Past history is the crux of my whole discussion. I suggest that the history-taker use a fairly definite formula, varied when necessary to suit the intelligence of the patient, as follows: "We realize now that many sicknesses are made worse by worry and fear and too much thinking and I must ask you to tell me whether you have had any mental or emotional distress from any cause. I will read you a list and ask you to say 'Yes' or 'No' to each. You need not give any details unless you wish.

Financial strain
Business problems
Legal complications
Social difficulties

Domestic or sexual difficulties
Religious difficulties
Fear of future events or acts
Fear of disease, physical or mental
Any undecided problem or conflict
Past shocking experience
Past grief or disappointment
Unspecified."

Par. 40. Habits: reading, study, rest, religion, recreation, hobbies, etc.

Par. 50. Family history of any "nervous breakdowns", eccentric characters, epileptic, defective, alcoholic, drug-using, insane or lawless individuals.

The obtaining of significant data, especially under Paragraph 30, calls for a consultation with the neuropsychiatrist.

It seems to me that the use of this proceedure in a medical service gives the intern valuable experience when the patient cares to talk freely, gives the patient an easy first step in unloading worry, and greatly betters the chances for catching mental elements early and dealing with them effectively.

Factors in the Prognosis of High Blood Pressure*

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WHEN discussion is undertaken of the prognosis or treatment of any pathologic state, the etiology of which is unknown, difficulties are at once met. To this rule arterial hypertension is no exception and more than one competent observer has stated that its satisfactory prognosis cannot be made. Such an attitude of avoidance, while safe, is for the clinician most unsatisfactory and in certain kinds of practical work intolerable. Is it necessary? It is the writer's opinion that experience has reached a point at which one may profitably attempt to set down in a concise way what has practical bearing on this difficult subject. One may use the philosophic method of approach, attempting to understand the fundamental nature of high blood pressure and from such a basis to reason its consequences; or the method of experiment—the study of the experience of others or of one's self in dealing with this malady.

From the viewpoint of physiology there appear to be two chief factors in high blood pressure; i.e. cardiac output and peripheral resistance. Of these the peripheral resistance seems the factor of dominant clinical importance. Through the sensitive vasomotor system, this peripheral resistance may be influenced by mechanical, chemical, nervous, endocrine, and other factors. However, until the physiologist gives more complete knowledge of the sympathetic nervous system and of the glands of internal secretion, the clinician must work under the handicap of partial and very limited command of essential facts in the etiology of high blood pressure.

Like other symptoms, hypertension may be associated with a variety of conditions. Chief among these are increased intracranial pressure, physical and emotional stress, aortic insufficiency, renal insufficiency, thyroid disorders, the action of such substances as adrenalin, pituitrin and ephedrin; certain toxemias of pregnancy, and some types of arteriosclerosis; in at least one of the last named, probably more as cause than effect. Since we are dealing only with prognosis, we can dismiss these types of what may be called secondary hypertension by the general statement that their outcome is that of the associated and underlying condition. This leaves for consideration from the standpoint of prognosis the great group of primary or essential hypertonias, so called because in it we cannot as yet find any associated or apparently causative condition.

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While our limited knowledge undoubtedly lists under the title essential hypertension conditions of varied etiology, most of the cases run true to type. In their physical characteristics, the patients are usually thickset and stocky, deepchested with broad hips and shoulders, short necks and round heads. They are likely to have thick skin, abundant and often heterosexual distribution of hair. Mentally they are serious, earnest, conscientious, enthusiastic at work, at their infrequent play, and too often at table. They are usually successful and, as Moschcowitz aptly says, they often "die of success". Of great interest is the remarkable resistance of this group to both major and minor infections. Because of the intensity with which they carry on, many of the world's leaders are found in this group. Rarely a thin, angular type will display a hypertension which seems to fall under the definition of essential hypertonia. The striking variation from the dominant type suggests that further study may reveal differences in etiology.

Can any satisfactory approach be made to the problem of the etiology of essential hypertension? Health is as dependent upon equilibrium of function as upon integrity of structure. Because of the difficulties in estimating function, too great emphasis has been placed upon structural changes in our definition and study of disease. Essential hypertension seems to be one of the few disorders in which an initial functional imbalance reveals itself long before changes in structure can be found.

The earlier view of Gull and Sutton, furthered by Romberg and others, that hypertension is secondary to a narrowing of the arterioles from arteriocapillary fibrosis has been largely superseded. The weight of competent opinion now holds that the high blood pressure precedes and probably causes the secondary changes in the vascular system. These changes are most pronounced and characteristic in the arterioles. Fishberg states that they consist in an irregular deposit of hyaline material directly under the endothelium, later undergoing lipoid change. In the larger arterioles there is hyperplasia of the internal elastic membrane with reduplication and formation of lamellae. Regressive changes follow with the appearance of hyaline and lipoid substance and a proliferation of connective tissue. The result is a narrowing of the lumen or obliteration. Fishberg further states that there is a progressive atrophy of the muscle cells of the media with hyaline and fatty changes and finally fibrous replacement rather than the hypertrophy more commonly described.

This same observer finds that these changes are by no means universal. The small interlobular arterioles and vasa afferentia of the kidney were found involved in 100% of the 72 cases examined at necropsy and the changes were more advanced here than elsewhere. Involvement of the arterioles of the spleen, pancreas and brain follow in this order of frequency. The vessels of the heart in essential hypertension show changes with surprising infrequency; those of the lungs, muscles and skin are almost unscathed.

If the concept of a primary functional vascular disturbance character-

ized by exaggerated vaso-constrictor tendencies with later and consequent organic changes in certain selected parts of the vascular tree be accepted, closer inquiry may well be made into the features of the earlier or functional stages that are capable of clinical demonstration. O'Hare and others have already called attention to this phase of hypertonia. O'Hare found the vasomotor system in hypertension very labile and sensitive. Excitation and exercise usually caused a marked and abrupt rise. The vessels in hypertonia were found extremely sensitive to adrenalin, very sharp rise in blood pressure taking place immediately after injection of this substance in the muscles.

The functional disturbances usually believed to be somewhat characteristic of this malady are

1. An ill balanced personality already described with the chief tendencies, pressure of activity and overearnestness.
2. Tachycardia, at first periodic, later more continuous.
3. Flushing.
4. Headache—often migrainous.
5. Vascular crises—usually episodes of mild anginoid pain, anxiety, palpitation or tachycardia with rise in blood pressure.
6. Undue or prolonged rise in systolic and diastolic pressure in response to emotion or effort.

To glean anything of prognostic value from study of such evidences of disturbed function is indeed difficult. The most tangible of these seems the rise in pressures following effort or emotion. Study of this and the pulse rate simultaneously gives certain data which can at least be expressed mathematically and may have some value.

One of the methods used in estimating the functional response of the circulation is the simple exercise test. Subjects' blood pressures and pulse rates are recorded while at rest. Exercise is then given to the point of beginning dyspnea when records are again made. Observations are then taken every minute for five minutes while the subject lies at rest.

No attempt has been made to make the test mathematically exact by having subjects of the experiment perform a measured amount of work. It is quite impossible to adapt such a test to all phases of circulatory disease, especially those in the advanced stages. A more universally satisfactory test for all types of cases seems the performance of enough work to bring about moderate dyspnea. This might be running up two flights of stairs for a youth in normal health or but a few liftings of the hands above the head for the bed-ridden patient with impending circulatory failure.

Study has been made of the response to an exercise test of this kind of normal individuals of different ages and of examples of hypertensive cardio-vascular disease. The latter have been divided into those in the early phases of the malady when no organic changes in the circulatory system were demonstrable, (Phase I); those with slight or moderate changes, (Phase II); and those advanced (Phase III) or terminal cases, (Phase IV), showing marked or extreme structural damage.

Without giving too much detail either in text or chart the results of

this study may be given schematically in Chart No. 1.

In harmony with the findings of Barath and others, it is apparent that in Phase I, the youthful normal, we have the ideal state of the circulation. In response to effort causing dyspnea, there is a moderate rise in systolic and a slight but definite fall in diastolic pressure. This results in a rise in pulse pressure which expresses the increased stroke volume output of the ventricle and a peripheral relaxation in response to the call for increased supply of blood to meet the demands of effort. The return to the previous or a lower level is prompt.

In Phase II we have the typical response of the individual in middle life or of one in early life with a beginning hypertonia. The rise in systolic pressure is more marked and the subsequent fall is less prompt and rarely to a lower level at the end of five minutes. Even in this early period of circulatory disorder the diastolic pressure is notably affected, tending to rise and to remain higher for some time after effort.

In the examples of established hypertension with slight or moderate structural changes in the vascular system, (Phase III), one meets the widest fluctuations in blood pressure in response to effort causing dyspnea. In some the changes in systolic pressure are extreme. The fall in systolic pressure is tardy and often at the end of five minutes the reading is above that of the previous resting level. The diastolic pressure in this phase is less variable. It may rise, but in my observation almost never falls as a result of effort.

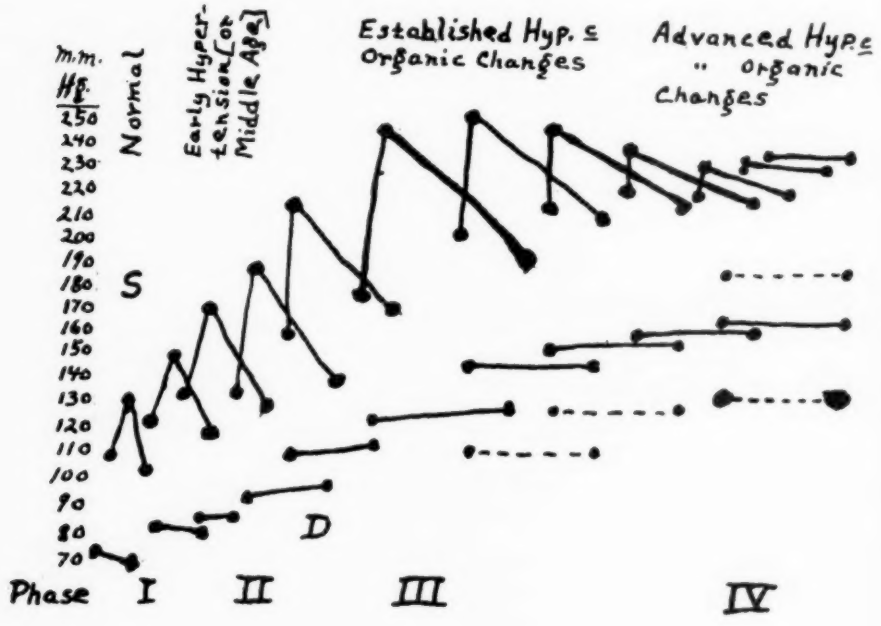

CHART I.

In the last group, (Phase IV), a very interesting fixation of both systolic and diastolic pressures is met. In this group are placed those who show marked arterio-sclerotic changes in retina, kidney or elsewhere in the vascular tree of a kind associated with a poor prognosis. We observe a fixation of both systolic and diastolic pressures at high levels with no variation as the result of exercise. Impression is that the circulation has been extended to the limit of its functional capacity even in conditions of repose and has no reserve by which it can increase its output to accommodate effort. It may be said that this type of response or the lack of it is found only in those showing the most extreme structural alterations in the vascular apparatus.

It is realized that observations of this kind are very rough and inexact; that there are plenty of exceptions to any rule in clinical work. Conclusions, however, are based upon a large number of observations chiefly from office practice made over a period of several years. It is believed that the functional response of the blood pressure to effort can be correlated with the degree of organic changes of the kind to be described in the second part of this paper in a manner that has some prognostic value.

Cases with a persisting fall in systolic pressure with a maintained or rising diastolic pressure are of serious import and indicate a weakening myocardium. In such, an added and not infrequent factor in an unfavorable prospect is a pulsus alternans.

ORGANIC FACTORS IN PROGNOSIS:

These have the greatest value. They are always present in any case of long standing or of fixed and marked hypertension. Upon their presence seems to depend the onset of the symptoms we associate with the more advanced phases of the malady under discussion.

1. CARDIAC FACTORS. These center about the functional efficiency of the myocardium. We know from the studies of Janeway, Allbutt, Paullin, Sprunt and others, that the majority of those with essential hypertension die a cardiac death. The most ominous condition in prognosis is that of congestive heart failure or circulatory stasis. Cases with this end result of hypertension and arteriosclerosis usually present a declining systolic and a lowered pulse pressure and, although they may rally for a time with proper management, the end is seldom far away. Auricular fibrillation following hypertension is usually of serious import. While I know of no statistical study on the point, experienced clinicians agree that angina pectoris when associated with high blood pressure, although always serious, does not carry with it the grave prognosis experience justifies in cases with normal or low pressure. It is possible that the greater vaso-motor instability of the patient with essential hypertension leads to the angiospastic type of angina which is less serious than that associated with the coronary sclerosis of a decrescent type, more often found in cases with normal pressures. Study of large groups of these two types of angina from the viewpoint of prognosis is needed.

VALVULAR DEFECTS: a. Mitral stenosis. Not infrequently this lesion of rheumatic origin is associated with hypertension. These patients seem to carry the lesion with comparatively little embarrassment from the hypertension. Perhaps the organization of the mitral valve prevents the development of the relative mitral insufficiency which is such a common feature of advancing hypertonia. The integrity of the myocardium is here the chief prognostic factor.

b. Mitral insufficiency when due to stretching of the mitral ring and attended by great enlargement of the left ventricle is always ominous. When there is no demonstrable dilatation of the left ventricle and the circulation is well maintained, a mitral systolic murmur may be passed over with the reservation that it may be a prophesy rather than a sign of weakened musculature of the ventricle. The cardiac capacity is the decisive point in prognosis.

c. Aortic insufficiency. When featured by a low diastolic pressure and a high pulse pressure this lesion in the presence of hypertension usually presages early disaster. This may follow sudden or gradual cardiac insufficiency or an anginal episode. Syphilitic cases with aortic insufficiency and hypertension must always be viewed with great concern. Those having rheumatic or other non-luetic etiology may carry on much longer. The myocardial capacity is again the final arbiter. The diastolic murmur is usually very loud and distinct in cases with low diastolic pressures. The examples of aortic insufficiency with normal or high diastolic pressures in the presence of hypertension usually reveal a very soft, barely audible diastolic murmur over the sternum. The origin of this murmur is probably in a very small defect in the mechanism designed to close the aortic orifice—either a slight stretching of the aortic ring or a slight retraction or rigidity of one or more cusps. An aortic insufficiency of this kind does not carry much weight in prognosis and for practical purposes can be almost ignored.

d. Aortic stenosis is a lesion of the elderly and, while it always presents the threat of a gradually advancing insufficiency of the left ventricle, may exist for many years with little progress. It is not often associated with hypertension.

2. *THE ELECTROCARDIOGRAM*. This has some importance in the prognosis of the myocardial changes following hypertension. Its value, however, is easy to exaggerate and it is of much less weight than the results of other methods of examination. When there are significant disturbances in the P-R time in the Q.R.S. complex or T wave, a bit of valuable confirmatory evidence is brought out. Apart from collateral facts, this may be unreliable for any final judgment and should always be subject to strict clinical control.

3. *THE PERIPHERAL CIRCULATION*. b. The large vessels. The aorta may be examined by ordinary physical methods or by the fluoroscope. Owing to the emphysema so often present in states of hypertension, the former methods are less reliable than direct visualization with the roentgen ray. The slight prominence

of the aortic knob at the junction of the transverse and descending aorta has little prognostic significance. Widening of the entire aorta with undue pulsation is only present in cases with extensive changes in the circulation. According to Sprunt such have a serious prognosis. Diffuse enlargement of the aorta, prominence of the aortic knob and dilatation of the descending aorta—all frequent in arteriosclerosis—are often mistaken for aneurysm by the inexperienced. Especially should one be wary of placing such an interpretation upon the bulging of the descending aorta just above the diaphragm. Physical evidence such as dullness beneath and beside the manubrium, undue pulsation here and in the episternal notch or a rough systolic murmur over the aortic area are usually present when there is significant variation from the normal. The non-syphilitic aortitis can usually be distinguished from that due to lues. Luetic aortitis is relatively rare in patients over 50 whereas the decrescent type is a feature of late middle or advanced life. In the syphilitic cases lengthening and bowing of the aorta and a tendency to sacculation is characteristic; aortic insufficiency with low diastolic pressure is more common, symptoms of circulatory disturbance more severe and the clinical and serological proof of syphilis usually obtainable.

Of the larger peripheral vessels those accessible to the examining finger are the brachials, radials, temporals, abdominal aorta, femorals, popliteals, internal malleolars and dorsales pedes. The brachial vessels are most readily palpated. The blood stream should be obliterated by pressure above and the character of the arterial wall estimated distal to the point of obstruction. Thickness, tortuosity and beading are the qualities of most significance. Changes of this kind in the larger arteries have little prognostic value. In persons used to manual labor, sclerosis of the large vessels of the extremities does not appear to influence length of life. Changes in the large peripheral vessels may be found as often with as without hypertension. These conditions seem not to have very definite relation. This is quite in contrast with the small vessel sclerosis as shown clinically in the retinal circulation. It is very exceptional that any well marked retinal arteriosclerosis is not attended by high blood pressure of long standing.

One type of hypertension needs emphasis. It has been well described by Fineberg. This is seen in the elderly with well marked sclerotic changes in the larger peripheral vessels and the aorta and with little or no apparent sclerosis of the smaller vessels as judged by ophthalmoscopic study. The peculiarity of the blood pressure is an elevated systolic and a normal or low diastolic reading. The left ventricle is almost always much hypertrophied and a relative mitral insufficiency frequent. The hydrodynamics of this type of hypertension seems to be the large stroke volume output of the hypertrophied left ventricle into a relatively rigid arterial tree and without undue vasoconstrictor influences. The disturbance is mechanical rather than functional, the changes are decrescent and largely primary rather than secondary. The usual ending is in cardiac

insufficiency. Evidence of the arteriosclerotic kidney is often found. Cerebral hemorrhage is infrequent. Cases of this kind have a comparatively good prognosis and may carry on for years.

(b). The Smaller Vessels; Although it is known that sclerotic changes may take place in one vascular field and not in others, much of general application may be inferred from the discovery of important local vascular pathologic changes. Especially in a condition in which the antecedent functional disturbance affects the circulation so universally, can the secondary vascular sclerosis when manifest in one series of vessels be with a high degree of probability considered typical of the condition of much if not all the analogous parts of the vascular system.

The fundus oculi is the field available for ready examination of the small vessels. If we consider the retina a prolongation of the brain through the optic nerve, changes in its circulation may with some reason be assumed to be also present in that of the rest of the encephalon. It is the writer's opinion that any survey of the cardio-vascular system that does not include a thorough ophthalmoscopic examination may be misleading as it is incomplete. Of as much importance as the discovery of the commoner retinal pathologic changes is the correlation of such changes with the other and more general findings. In this the medical man has a great advantage over the specialist. The practiced internist is quite capable of judging the character and extent of most retinal vascular changes.

Vascular Spasm. This is a debatable condition but from close study of many fundi the writer is convinced that patients with early essential hypertension present frequent variation in calibre with a tendency to contraction of the retinal arteries and with this a varying degree of pressure upon the retinal veins at the crossing of vein and artery. This has been noted particularly in a prolonged study of cases presenting the hypertensive type of the toxemia of pregnancy where hospitalization and close observation have been possible.

It may be said that vascular spasm when present with a labile blood pressure serves as a suggestion or prophesy rather than as an established fact of peripheral vascular changes.

Tortuosity of the Arteries. This is of two kinds. One may involve the larger vessels alone as wide, sweeping curves often without other evidences of vascular change. This does not necessarily imply an arterio-sclerosis. The other involves the smaller vessels along with the larger in curves of small radius so that the vessel is of a somewhat corkscrew form. Such tortuosity almost always implies serious vascular change.

Increased Light Reflex. Widening of the central streak of light along the course of the artery especially when combined with a striking change in color to a silvery sheen or forming an almost white band, often of varying width, is of considerable import when associated with other changes.

Variation in calibre and contour of individual arteries is often patent to the practiced eye and is of importance in prognosis. This change seems particularly but by no means exclusively

a feature of cases with syphilitic background.

Constriction and displacement of veins at the crossing of arteries is one of the easiest changes to detect and one of the most significant. This may vary from the slightest indentation such as may transiently mark the spastic cases to an apparent entire cutting off the venous stream and the sharp lateral and segmental displacement of the vein.

White patches may be of two kinds. One type is made up of small white flecks or wedgeshaped minute spots rather diffusely scattered over both retinae. These seem to be associated with comparatively benign types of hypertension. The other kind is characterized by a few large white areas at times reaching half the diameter of the optic disc. These are often attended by hemorrhages or marginal flecks of black pigment, evidence of former hemorrhage, and seem to attend the more serious examples of vascular disease.

Hemorrhages, whether small or large, when attended by definite sclerotic changes in the arteries are always serious and are one of the most valuable of prognostic signs. To be sure, one must differentiate the hemorrages of inflammatory and toxic origin unattended by arteriosclerosis.

Thrombosis when attending serious vascular degeneration may be placed in this same category with hemorrhage.

The Central Nervous System: Evidence of vascular degeneration in this important field can be inferred from like changes in the retina and from certain results of impaired circulation. The latter are the probable consequence of ischemia from vascular spasm or from thrombosis or hemorrhage. These may be transitory or permanent. They may vary from momentary vertigo or aphasia to passing or permanent mono- or hemi-plegia, or a vascular accident serious enough to result in death. Although minor attacks of cerebral ischemia may occur several years before death they are usually among the most ominous of the consequences of vascular disease. The changes in mentality characterizing arteriosclerosis are not to be passed over in considering prognosis.

The visceral circulation especially that of the kidney and pancreas may be sufficiently altered as to disturb the function of these important organs in a readily recognizable manner. In the presence of widespread cardiovascular disease the finding of a high specific gravity, marked albuminuria with numerous red blood cells and hyaline casts is good evidence of an arteriosclerotic kidney. Usually there is a moderate increase of uric acid in the blood in cases of this kind. Only in the later stages may there be retention of nitrogen. Such retention may be due to cardiac insufficiency, to superimposed inflammatory degeneration of the kidney or to coalescence of enough foci of anemic necrosis through arteriosclerosis to abolish the factor of safety in the kidney. Tests of renal function here as in other conditions are of no value until this factor of safety is abolished. It may be said in general that established signs of an arteriosclerotic kidney usually attend examples of advanced cardiovascular disease and, therefore, make for a grave prognosis. One fact needs emphasis;

cases of essential hypertension rarely die from uremia.

It may be said that the mild diabetes of later life so often found with arteriosclerosis has for its basis arteriosclerotic changes in the vessels of the pancreas. O'Hare found such changes in a considerable percentage of examples of cardiovascular disease with hypertension. Glycosuria, since it usually attends advanced cases, is always a serious factor in prognosis and seems to have about the same weight as the manifestations of the arteriosclerotic kidney.

Summary

The salient points in the prognosis of high blood pressure may be summarized. Unfavorable features are a family history of cardiovascular disorders, a relatively high diastolic pressure and, chiefly, evidence of degeneration in certain selected parts of the cardiovascular system. These evidences are of marked arteriosclerotic changes in the cerebral, retinal, coronary, renal or pancreatic arteries or in the aortic arch. Signs of myocardial weakness make for a bad prognosis. Among the functional tests, that revealing a lack of normal response to effort on the part of pulse rate and blood pressure, when existing with advanced structural changes in the circulatory system, is a not unimportant item in an unfavorable prognosis. This is especially true where both systolic and diastolic pressures are fixed at high levels and do not vary after effort.

Of the favorable features the following may be mentioned. High blood pressure in the absence of demonstrable organic cardiovascular changes may not shorten life. This is especially true of cases in women appearing about the time of the menopause. High blood pressure with predominant changes in the larger peripheral vessels and with little change in the aorta or retinal vessels may be viewed with much less concern than those with marked changes in the smaller arteries. This is particularly true of cases with normal diastolic pressures and of those without albuminuria and glycosuria. Cases retaining their capacity to respond by a normal or exaggerated rise in blood pressure after effort carry a better prognosis than do those in which this capacity has been lost.

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Arterial Hypertension*

By George C. Hale, *London, Ontario*

ARTERIAL hypertension, according to the dictionary, means abnormally high blood pressure. Now the original comprehension of the term, blood pressure, was the pressure of the blood upon the arterial wall such as would be recorded by a canula inserted into an artery and attached to a manometer. This is not practical from the clinical point of view, and as the possibility of error in the estimation of this pressure by the clinician's finger was great, the sphygmomanometer, or blood pressure apparatus with which we are all familiar, was introduced and has come to be a part of almost every physician's armamentarium.

However, with this apparatus there is liable to be considerable error for the following reasons—When we attach the armlet and inflate it sufficiently to obstruct the flow of blood so that there is no radial pulse, we are not only measuring the pressure of blood upon the arterial wall, but the pressure necessary to compress the wall itself sufficiently to obstruct the blood flow. In other words, a certain measurable pressure is required to compress the walls of an artery sufficiently to prevent the flow of a fluid not even under pressure. Experiments with an artery removed from the body within two hours after death and before the vessel had lost that tonicity of wall which the living muscular coat gives it, have proved that a pressure as high as 100 mm. mercury may be necessary to compress the wall sufficiently to prevent water flowing through by gravity.

An artery removed shortly after death of the patient will contract and thicken by mere handling and it is probable that the same phenomenon occurs when pressure is exerted during life by the armlet of the sphygmomanometer. This thickening of the wall and narrowing of the lumen would necessitate greater pressure to compress the vessel with consequent rise in the estimated systolic blood pressure. As the artery tired and relaxed the pressure would apparently fall. Here may be the explanation of the frequently observed fact that if the blood pressure is taken three times in succession, the third reading will be lower than the first. So when we measure systolic blood pressure clinically the factors with which we are concerned are not only peripheral arteriolar resistance, but the consistency of the wall and the internal calibre of the brachial artery.

*Read before the Boston Meeting of the American College of Physicians, April 10, 1929.

When the ventricle ceases to contract and passes into diastole, the blood pressure does not cease but there is a recoil by the artery wall which, as it were, passes the blood forward with a measurable pressure called the diastolic blood pressure. The second bulb in the scent spray, the bag of the bagpipes, and the compression chamber of the fire engine together with a nozzle in each instance provide a similar arrangement for maintaining a constant flow at a given pressure.

Normal systolic blood pressure is given variously in text-books as from 105 to 145 mm. of mercury; normal diastolic pressure as from 20 to 50 mm. lower, making the normal so-called pulse pressure 20 to 50 mm. Various conclusions have been set forth by writers regarding the significance of the pulse pressure, but it is a question whether these are justified in dealing with such a variable factor.

Without going further into the question of the accuracy of our methods of determination of actual blood pressure, or the importance of diastolic pressure and pulse pressure, let us consider the question of the significance of high blood pressure, or arterial hypertension.

For many years its presence in cases of nephritis or vascular disease was not considered strange, and was explained as resulting from a call on the part of nature for a rise of blood pressure to enable sufficient blood to be forced through the sclerosed kidneys or through arterioles of lessened calibre, just as more pressure is required to force water through rusty pipes of diminished lumen.

Only in comparatively recent years has arterial hypertension been unmasked and recognized, not as a disagreeable, but necessary result of nephritis and arterio-sclerosis, but in many cases a traitor guilty of actually causing these two diseases with which it is so frequently associated.

As a result of this unmasking, cases of arterial hypertension were studied from a new perspective, the wood was finally discovered in spite of the trees, and instances were reported of death from this disease without autopsy findings of nephritis or vascular pathology.

Let it be granted that arterio-sclerosis can cause arterial hypertension and that the latter may be due in some instances to renal arterio-sclerosis, to arterio-sclerosis of the medulla as suggested by Starling, or even to coronary sclerosis and so forth, there still remains a large group of cases which cannot be explained by such means and where the etiological factor remains obscure.

To this entity of idiopathic or essential hypertension the name of hyperpiesia was first applied by Sir Clifford Allbutt. His original definition reads as follows—"Hyperpiesia is a malady in which at or towards middle life, blood pressure rises excessively: a malady having a course of its own, and deserving the name of a disease." He goes on to say—"Of hyperpiesia I have never offered an explanation or nothing more than conjecture. I have been content to distinguish it as a clinical series from recognized forms of Bright's Disease."

There are some who still hold to their former tenets that hyperpiesia is the result of precursory renal pathol-

ogy because it is so frequently accompanied or closely followed by evidence of disturbed renal function. The latter is to be expected, as is evidence of pathological changes elsewhere resulting from secondary arteriolar fibrosis, if the scientific eye were not focussed so persistently on the kidneys to the exclusion of other organs. Batty Shaw reports nineteen cases of hyperpiesia which died with clinical evidence of uremia. Of these there were three cases which showed no renal change whatever. He argues that uremia was impossible in these three cases, and by deduction improbable in the other sixteen. To properly evaluate this statement, however, one would have to be sure just what is meant by the term uremia, a question which suggests depths too deep to plumb in this short address.

The difficulty in studying the pathology of those dying of hyperpiesia lies in the fact that few actually die of this condition, but rather from the effects of continued hyperpiesia upon the arterial system. In cases dying early from some intercurrent disease while suffering from hyperpiesia, the picture is liable to be clouded by the effects of the intercurrent disease on the organs.

Much experimental work has been done in an attempt to discover the probable origin or identity of some pressor substance in the blood capable of producing the vasomotor excitability and resulting sustained arterial spasm which we call hyperpiesia.

Search has been made for some abnormal pressor substance produced by disturbed metabolism, or normal substance produced in undue amount, or in normal amount but acting on a hypersensitive sympathetic nervous system.

In connection with faulty metabolism it is of interest to note the frequent relationship of obesity, diabetes, and gout to hypertension; and to recall the pressor effect of guanidin and creatinin, which may be produced in relatively large quantities by perverted metabolic action.

The endocrine system has been considered as a probable factor due to the occurrence of hypertension during the menopause and in hyperthyroidism, and also because of the well known effect of adrenalin on blood pressure. The suprarenal glands, however, are not enlarged in hypertension, and no one as yet has succeeded in demonstrating adrenalin in the blood in this disease.

Working on the theory of pressor substances being produced as the result of degeneration or disease of certain organs such as kidney, liver, spleen, etc., investigators have made extracts of these and injected them into animals and humans. The main effect in every instance, except that of kidney extract, has been a depressor and not a pressor one, i.e., the blood pressure was lowered. The fact that kidney extract can exert a pressor effect might explain the hypertension in some cases of chronic nephritis, but it does not offer a solution as to the cause in those cases where at autopsy the kidneys have been found normal.

Certain results are inevitable in continued hypertension. 1. The heart hypertrophies, as one would assume any muscle would do in response to a demand above the ordinary. If the my-

ocardium is healthy the heart may remain competent for many years or permanently unless peripheral resistance becomes too great, when the organ, sound though its muscle may be, finds itself unable to force blood against this enormous resistance; capillary stagnation supervenes, and the patient dies of cardiac defeat. If the myocardium is diseased the owner may succumb to an early cardiac death. 2. The arterioles undergo a sclerosis, due either to the inordinate strain to which they are subjected, or to an unknown toxin, or both. This means, as far as the organ or tissue supplied by the sclerosed vessels is concerned: (a) less blood, (b) less gas and chemical exchange, (c) less detoxication, resulting in (d) accumulation of waste products, (e) less efficiency and coordination, (f) more fatigue, with the end result of atrophy and fibrosis of that organ.

The clinical picture will depend on which organs are chiefly affected by this arterio-sclerotic process, and the most characteristic pictures are those in which the greatest sufferers are the cerebral, coronary, or renal arterial systems, giving us the syndrome we characterize as apoplexy, angina pectoris, or azotemic nephritis.

It is of interest to note that, in spite of the agreement of the almost universal affection of the renal arterial system in hypertension, Romberg reckons that 45% of cases die of heart failure, 45% of apoplexy, and only 10% of uraemia.

There have been many attempts to classify hyperpiesia clinically without much success. Probably the most popular classification is that of benign and malignant hypertension. Rowntree defines malignant hypertension as occurring in about 10% of all cases, of an unknown cause with a stormy and rapid progress; the diastolic blood pressure disproportionately high, neuroretinitis common, and cerebral renal and cardiac symptoms frequent; the prognosis grave, and treatment unsatisfactory. It would be impossible to classify hyperpiesia clinically from the height of the systolic blood pressure, as has been suggested, as cases of undoubted and previously proven hypertension may show normal blood pressure some months before death. In fact, pathologists usually assume that primary hypertension was present in life when at post mortem examination is found a high degree of left ventricular hypertrophy not associated with valvular disease, adherent pericardium, syphilitic aortitis, chronic glomerular nephritis, or hyperthyroidism.

Writers of an imaginative turn of mind have attempted to describe a human type as prone to develop hypertension. The disease, however, is too protean to allow of such easy characterization. We have all encountered it in the sallow, intense, and tired business man, in the choleric and ruddy squire with his foot bound up in a pillow, and in the pasty and lazy fat boy of Dickens now grown up.

Hypertension, like diabetes, is especially vicious in early life and relatively benign in the elderly. It is, however, the early cases, before the occurrence of arterio-sclerosis, which respond most favorably to treatment. With regard to elderly arterio-sclerotic cases who have had moderate hyper-

tension for many years without the occurrence of grave symptoms, adopt the attitude of Joslin regarding diabetes. Joslin says, "If a diabetic has known enough to live ten years, be sure you know enough to make him live another ten years before you tamper with him. The old diabetic has arteries so hard that his status must be changed as delicately as you would move a choice piece of bric-a-brac." The same rule applies to the elderly arteriosclerotic with high blood pressure. Many of them undoubtedly have an optimum blood pressure below which they cannot be forced without disaster.

The question of treatment of hypertension covers a very large field including as it must many associated or terminal conditions such as hypertension plus apoplexy, plus angina pectoris, plus uremia, etc.

Treatment on the whole is unsatisfactory. This is to a certain degree due to the following facts—(1) A large percentage of cases will show a temporary fall of blood pressure with each new doctor consulted, or each new treatment tried. (2) Many of the remedial agents cause a purely temporary drop of blood pressure at the time of their exhibition. (3) In many instances, if one succeeds in lowering the blood pressure, the patient feels much worse.

If there is some readily ascertainable and removable cause such as focal infection, intestinal intoxication, obesity, abuse of alcohol or tobacco, or a misconception on the part of the patient as to the amount of work and worry that is his share in this world, there may be some cause for optimism on the part of the physician. If, however, the removal of such causes does not lead to improvement, the results will be disappointing.

Time and space do not permit one to go into detail regarding the present status of such therapeutic agents as therapy, etc. Each has its optimists, liver extract, the sulphocyanates, veratrum viride, diathermy, hydro- its pessimists, and its merely hopefuls!

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Radiation Therapy in Malignant Disease—Results To Be Expected*

By George E. Pfahler, M.D., *Professor of Radiology in the Graduate School of Medicine of the University of Pennsylvania, and Chairman of the Committee on Cancer Control of the Philadelphia County Medical Society, Philadelphia*

WITH our present knowledge of the treatment of cancer, *good results can only be obtained by the early recognition of the disease and by the immediate, thorough and skillful treatment. The fear of operation on the part of the patient is an important factor in causing delay.* If this fear can be eliminated by the family physicians and the consultants, who know that radiation is of definite value in the treatment of malignant disease, patients will be more likely to consult the family physician at once, instead of going to quacks, or doing nothing. Postponement is most often due to fear of operation, or failure to realize the seriousness of the disease, and also due to the *absence of pain in the early stages.* It has seemed to us, therefore that a review of the results that have been obtained or that may be expected under given conditions should be of value to you as consulting internists. In this study, we must take into account our limitations as radiologists as well as our possibilities.

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Skin Cancers

Practically all or approximately 100% *of cancers of the skin* can be cured by means of radium, x-rays, or electro-coagulation or by a combination of these methods, providing they are treated skillfully while they are still only cancers of the skin. When, however, the ordinary basal cell cancer of the skin (which can certainly be cured at the beginning) has invaded the deeper tissues, such as the cartilage or the mucous membrane of the nose, or fascia, muscle or bone, it then becomes a very difficult matter and requires the greatest skill and ingenuity.

It is supposed by some that practically all skin cancers are of the basal cell type and that they do not give rise to metastasis. This is a mistake. Most cancers that develop on the hands or in scar tissue, and those developing in the temporal and zygomatic regions are very apt to be of the squamous cell type and they give rise to metastasis. Therefore delays, or inefficient treatment at the beginning *of cancer is dangerous.* The *pigmented mole* that has undergone malignant degeneration is the most dangerous of all and *should be destroyed by electro-*

coagulation completely at one sitting, at the very beginning. There is sufficient means now available to remove moles easily, and satisfactorily, and it would seem advisable to have all moles removed for cosmetic reasons as well as for future safety, on the same basis that one carries fire insurance—even though probably not more than one in a thousand becomes malignant. Radium, x-ray treatment, or excision caustics are not satisfactory in the treatment of pigmented moles.

Epitheliomata about the eyelids are best treated by radium, or next best by the x-rays. Electro-coagulation is apt to lead to ectropion and is therefore less satisfactory. Excision often fails to eliminate all of the disease, probably due to the necessary attempt to conserve tissue.

Epithelioma of the Lip

In 82 primary cancers of the lip, without palpable lymph nodes, which were treated by electro-coagulation, by us, combined with high voltage radiation over the glandular area, 97.5% were cured. This illustrates the importance of thorough treatment at the beginning.

When the lymphatics are definitely involved, the only hope from radiation treatment is by the use of highly filtered gamma radiation, and sometimes combined with operation. *The results by means of any form of treatment or any combination will be less and less satisfactory, the more the disease has extended.*

Cancer of the Mouth

The results from the most skillful radiation treatment of cancer of the mouth vary so much with the stage of the disease and its location that it is difficult to make an accurate estimate briefly. The general average of all cases applying for treatment in all stages at which they now come under skillful treatment is about 25% of cures.[1] If these same patients can receive skillful radiation treatment *when they first come under the care of a physician*, at least 50% should be cured, and *if patients can be educated to apply for this treatment when lesions in the mouth first appear, at least 75% should be cured.* In a review of the work done at the Radiumhemmet, at Stockholm, Forsell,[1] found 62, 62, and 56 per cent after one, three, and five years respectively, in primary operable tumors. In cases with regional metastasis he advises operation combined with radiation, and by this combination obtained cures in 35%. Häggström's[2] surgical statistics, the figures of which do not fall below those of other statistics published on the same subject, show 31% of healings with lasting effect for five years (20 cases out of 64). The corresponding figure for exclusively radiological treatment of operable primary tumors is 56% (16 cases out of 29), and for the combined surgical and radiological treatment 60% (13 of 22). It is clearly evident therefore that radiation alone, or radiation combined with surgery is the best form of treatment in cancer of the mouth in the operable stage. Forsell, makes the following observations:

"1—With radiological healing the percentage of *recurrences* is very low when once complete freedom from

clinical symptoms has been obtained and has been maintained for one year.

2—With the technique employed, and with the clientelage represented, a permanent healing was only obtained in those cases in which the disease was still macroscopically confined to its primary site. In none of the 72 cases in which there was unmistakable regional metastasis to the lymph nodes, was healing obtained for as much as one year." (In all these cases, the glandular metastases were very extensive, they were inoperable, and in poor general health).

In 68 primary, *operable and inoperable cases*, without palpable lymph nodes, there were 31% five year cures, in Forsell's records, Buchanan,[3] gives 20 months as the natural duration of cancer of the tongue.

My records as reviewed by Dr. B. P. Widmann show: Primary Carcinoma of the tongue with no lymph nodes, 55% were well from 4 to 15 years. Primary Carcinoma of the *Tongue, with lymph nodes*, 40% are clinically well from 1 to 5 years. Unless the glandular involvement is very extensive, we think the chances of recovery are fairly good. Counting *all the tongue cases, of all grades, 23.6% are apparently cured*. In our group of 78 carcinomas involving the inside of the *cheek*, 15 were too far advanced for any kind of treatment, leaving 63 cases for classification. Among these 63 cases the alveolar process was involved in 28 cases. Of 20 primary cases, with no glands, 13 or 65% recovered. Of these 13 that recovered, two died of intercurrent disease and the other 11 cases or 55% are well from 1 to 15 years. Carcinoma of the cheek with glands showed 11% well 3 and 5 years. It seems to me that from 50% to 75% of all cancers of the inside of the cheek as they first come to the physician should be cured, if treated thoroughly and skillfully at once by gamma radiation.

Cancer of the Tonsil

Cancer of the tonsil is infrequent as compared with other malignant lesions about the mouth. Matthews[4] concludes that practically all cases are *surgically inoperable*. The prompt recurrences following surgery in the apparently locallized lesions, indicates that there is usually widespread infiltration at the base. With tonsillectomy alone, in 20 cases of sarcoma and 3 of carcinoma, not one was reported to have lived 2 years without recurrences. On the other hand, *malignant* disease of the tonsil seems to be rather sensitive to radiation. Schriner,[5] reports 15 cases with no gland involvement and of these one case was clinically well after radiation. Forsell,[6] reports on 31 cases with 9% clinically cured. Quick,[7] reports on 124 cases of carcinoma of the tonsil, with 22.5% clinically cured by radiotherapy for an average duration of 26 months.

Our Statistics

In our group of 24 cases of carcinoma of the tonsil, 3 cases were too far advanced for any kind of treatment. Of 3 primary cases without palpable lymph nodes all are clinically well 1½, 3, and 4 years, treated by the *saturation method* of roentgentherapy. Of 8 primary cases with metastasis, one is well 7 years, one which was clinically well died of intercurrent dis-

ease. All of the recurrent cases died of the disease.

It would seem advisable to treat all malignant disease of the tonsils by gamma radiation, or if not recognized until after operation to give immediate post-operative treatment, locally and externally by gamma radiation.

CARCINOMA OF THE BREAST

Cancer of the breast is a surface growth which should be recognized in its earliest stage. If removed surgically while it is strictly confined to the breast, theoretically there should be 100% cures. Practical experience however, shows that only about one out of five reach the surgeon in this early stage, and that as a matter of fact even in this supposed early stage only about 70% are cured.

Four-fifths of the patients reach the surgeon only after the disease has extended at least to the lymph nodes in the axilla and of these surgery shows approximately 22% cures, when radiation is not added. *When radiation is added to operation we may expect approximately* 46% *cures,* or about twice as many cures as from operation alone. In a review of 1066 privately treated cases of carcinoma of the breast we,[8] found 68% of the early operable cases living at the end of 5 years and of the late operable with gland involvement 46% were alive at the end of 5 years when radiation and operation was used.

Comparative Values of Other Clinics and Methods. (*Operable Cases*)

		Alive 3 years		*Alive 5 years*	
		No Glands Percent	With Glands Percent	No Glands Percent	With Glands Percent
Greenough	Surgery	47	19		
König	"			100	39
Bloodgood	"			70	20
Lee	"				15
Finsterer	"				4.3
Doederlein	"			46	5
Doederlein	" and radiation not completed			48	20
Doederlein	" and radiation totally completed			80	48 36
Wintz	" and radiation both groups 77%			64	42
Schmitz	" and radiation			68	46
Pfahler & Widmann					

Upon theoretical grounds, I have been recommending pre-operative treatment during the past 12 years, and post-operative treatment during 25 years.[9] Now some brilliant experimental work has been done by Murphy,[10] and his associates at the Rockefeller Institute, and by Russ and Scott,[11] in London in which experiments they exposed only small areas of tissue with 50, 65, and 100% of an erythema dose, leaving a central area unexposed. They then innoculated Jensen's rat sarcoma into this central area and in all instances the tumor grew in the unexposed tissue leaving to a great extent the areas treated in advance by x-rays uninvolved. To me these experiments are very convincing, as to the value of pre-operative treat-

ment. Clinical proof is shown by our own experience, and also by Forsell, at the Radiumhemmet in Stockholm, in which he gave pre-operative treatment to 169 cases and 51.5% were free from symptoms from 1 to 7 years. It seems therefore, to be definitely shown that radiation combined with operation may be expected to double the cures obtained by operation alone; that radiation will give much palliation in inoperable cases; and that some inoperable cases can be made operable.

CARCINOMA OF THE UTERUS

Cancer of the uterus like cancer elsewhere in the body is best treated in its early stages, or better treated by eliminating precancerous conditions. *If all lacerations are properly and promptly repaired; all cervicitis thoroughly treated and any vaginal discharge investigated at once, many cancers will be prevented.* If to this a thorough periodic health examination is made biannually of women, especially after 35 years most cancers of the uterus will be recognized in an early stage, when we may expect from 50 to 80% of cures by thorough radiation. In fact, in the report by Seuffert,[12] from the Doederlein clinic in Munich, it was found that the operable cases who had followed through the complete treatment, 80% were well at the end of 5 years. This then is the best chance for the woman who comes early and has thorough and complete radiation treatment. When one studies the general average of all patients who come to a clinic for treatment, the results are not nearly so good.

In the report of the Ministry of Health in London, published 1927, Dr. Lane-Claypon in comparing statistics of 6,661 cases operated on either by vaginal or abdominal hysterectomy, 2,272 were alive at the end of five years, making 34.1%. In the case of 1.117 "Operable" cases treated only by radiation, 400 were alive at the end of five years, which equals 35.8%. The end results, therefore, in a large series of operable cases are about the same, but with operation there is an operative mortality of 17 per cent.

Of all cases who presented themselves for treatment, operable and inoperable, 18.3% were alive at the end of 5 years, while radiation of a similar group gave 22% of 5 year results.

Ward and Farrar,[13] studied a total of 134 cases treated by radiation from 1919 to 1923 and at the end of 5 years 23.1% are living. Of the 32 operable and borderline cases in this series, 53.1% are living.

The earlier, the more thoroughly, and the more skillfully cancer of the uterus is treated, the better will be the results no matter whether it be by operation, or radiation. There is no other practical method known. The choice as to operation or radiation in any particular case will depend somewhat upon the skill and facilities available; but this choice can only be applied to the operable cases. In the surgical clinics the operable cases are 57% and in the radiological clinics the operability is 29%, leaving 33% and 71% respectively that can only have a choice between radiation or nothing. From a study by Heymann,[14] of 19 operative clinics, the operability rate

was found to vary from 81 to 15.7% or an average of approximately 57% while in 13 radiological clinics, the operable cases varied from 51 to 15.3% or an average of approximately 29%. It will be seen therefore that a very much more favorable group of cases is seen in surgical clinics. It is likely that in considering surgery the family physician decides in many cases that the patient is inoperable and does not send the patient to the *surgical clinic*, while all classes are sent to the *radiological clinic*. This is a compliment to radiotherapy, but tends to lower the total statistical values.

Even in those gynecological clinics, (Baisch, Doederlein, Menge, Kehrer, Wintz) in which surgery was abandoned for radiotherapy and in which the same methods of classification were utilized, the percentage of operable cases was very much lower and a more hopeless class of patients applied for treatment when it became known that only radiological methods were used. In Doederlein's clinic, for example, 265 cases of cancer of the cervix applied for treatment during the 5 years including 1908 and 1912, of which 63.02 percent were operable, while surgery was used; and in the years of 1913, 1916, when radiation was adopted, 500 cases applied of which only 33.9% were operable—about one-half as many were operable but about twice as many patients applied for treatment in a similar period. The fear of operation causes much delay and when it is known that the earliest cases have even a better chance with radiation therapy, patients will apply for treatment earlier. For example, at the Radiumhemmet in Stockholm, the operability rate has risen from 29.1% in 1921 to 59.2% in 1925.

From a study of the statistics from 20 of the leading gynecologic clinics of the world in which *surgery* was used, and in which 5,805 patients applied for treatment, there were 19.1% of five year cures. This percentage drops to 18.7%, if the study is confined to the eleven largest clinics in each of which there is recorded at least 200 applicants.

From a study of the statistics from 17 radiological clinics and counting all applicants 3,512 there was obtained 16.3% five year cures. In comparing the results of 19.1% from surgery, with 16.3% from radiation therapy it must be remembered that *the radiological material only contains about one-half as many operable cases.*

The primary mortality in 3,257 cases of cancer of the cervix operated upon in 24 leading clinics was 17.2%. The primary mortality for radiological treatment is usually considered negative, but Heyman, in reviewing the 502 cases treated at the Radiumhemmet found 8 patients or 1.59% who died in immediate connection with the radium treatment.

If one confined the statistics to the operable and borderline cases only it is found from a review of 24 of the leading surgical clinics in which 3,659 cases were operated upon, there is a five year recovery of 35.5% while 12 radiological clinics gave a general average of 34.9%. In the radiological treatment of 145 cases at the Radiumhemmet in Stockholm, there were 5 year cures of 46.2%.

In dealing with the operable cases, with radiological treatment, it must

be borne in mind that the treatment involves relatively little inconvenience, as compared with an extended operation and that while 54% are not well at the end of five years, the majority of these 54% of patients have palliative relief, and may be free from symptoms for one or more years; and that the immediate mortality is eleven times as great from operations as from radiation.

Only a few statistics give a statistical account of the morbidity either from operation or radiation. Davis,[15] reports 17 cases of primarily healed abdominally *operated cases* with the development of urinary fistulae in four cases (25%) and another four cases developed pyelitis, thrombosis, cystitis and suppuration respectively, and Gaydoul and Schmidt,[16] report from Hofmeier's clinic five cases of damage to the urinary tract among 50 *abdominal operations*. Among 502 cases treated radiologically at the Radiumhemmet from 1914-1921, 54 cases, 15% gave some rectal reaction (tenesmus, pain, bleeding from the bowel, impaired general condition, fever) with ulceration in 13 cases, and the fistulae only (1%) result in permanent inconvenience. The deaths (1.59%) occurred in the septic cases from peritonitis.

The palliative results obtained by Heyman, in 375 patients which were not well at the end of 5 years and which are counted a failure obtained relief from hemorrhage in 90% with 23.4% remaining free after 2 years. Pain was relieved in 53% and 28% remained free at the end of 2 years. Of 231 cases unable to work at the beginning, 61.6% were returned to work and 30.3% remained at work at the end of 2 years.

It will be seen therefore, that all in all, radiological treatment when applied skillfully gives the better results in any stage of cancer of the cervix.

CANCER OF THE UTERINE BODY

In most statistics cancer of the body makes up about 10% of the total cases of cancer of the uterus. In nine surgical statistics, studied by Heymann, the operability percentage varied from 62 to 100% and the five year cures varied from 24.0 to 59.1% or an average of all applicants (318) of 42.8 percent; and 58.8% of only operable cases are counted. Of the total number of cases (46) treated by radiation at the Radiumhemmet from 1913 to 1921, 45.7% were well after 5 years, while if only the operable cases (25) are considered 60% were well after 5 years, when treated by radiation. Therefore, it will be seen that the end results from skillful operation or skillful radiation is approximately the same.

Time will not permit the discussion of cancer in all parts of the body. The subjects which I have discussed cover the fields in which radiation has been shown to be of superior value. In my opinion, however, we may summarize the subject as follows:

1—Cancer of the *skin* can be cured by electro-coagulation and radiation in practically 100%, if treated early.

2—Cancer of the *mouth* should be cured in from 50 to 75% of cases in the early stage.

3—In cancer of the *breast* 45 to 75%

should be cured with operation combined with radiation, if treated early, depending upon the extent of the disease.

4—Cancer of the uterus should be cured by radiation in from 45 to 75% if treated thoroughly and skillfully in the earliest stages.

5—Cancer anywhere in the body can generally be retarded by radiation, but in visceral carcinoma, operation should not be delayed for radiation, but on the other hand all operations for cancer should be followed by radiation, either with radium or x-rays depending upon the condition.

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Can or Will the Internist Practice Preventive Medicine?*

By George H. Bigelow, *Boston, Mass.*

IN the presence of the clinician the health officer is apt to feel a self-conscious gratitude; "gratitude" because of the satisfaction that comes from mingling with those in the more established and time honored branches of the profession; "self-conscious" because many of the profound social, economic and medical readjustments with which the doctor is faced are blamed on the health officer and his ilk. But it is important that such mingling should not only be allowed but encouraged, in order that each may understand the profound difference of their points of view. The doctor must use every resource to protect the individual from his environment, while the health officer must in his turn strain hard to protect the environment from the individual. It is the same telescope but they are looking through it from different ends. But the world is full of profound differences in points of view: the lawyer and the judge; the autoist and the traffic officer; the commercial drug house and the pharmacologist; the mortician and the clinician; the cosmetist and Mr. Zeigfield; the bootlegger and the prohibitionist. Just think of the benefits that would come from an address by each of these conflicting groups to the other. Antithesis might become synthesis. Yet perhaps that might in the end be undesirable!

Let me illustrate the divergence in point of view of the practitioner and the health officer from our recent experience. We are profoundly interested in identifying and controlling the typhoid carrier. A member of a family in which there is a case gives a history suggesting typhoid fever twenty years ago. Yet the doctor is unwilling that we should examine specimens because he has "known her for five years". Physicians advise against typhoid prophylaxis of other members of the family, although half our typhoid is secondary. Dr. X agrees to report his communicable disease provided Dr. Y will do the same. Each waits for the other to start. Toxin-antitoxin is ridiculously little used in private practice though diphtheria still kills more children than automobiles. An occasional doctor talks of "state medicine" when the health officer strives for adequate examination of the children in the family of a tuberculous. Yet only 20 per cent of the tuberculosis in Massachusetts is reported in a favorable stage of the disease! In venereal disease control the con-

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flict in point of view is often the most readily apparent. One of the principal causes of white hair among health officers is the practitioner who varies his advice as to length of quarantine as he goes along. "There is the law", you say. But how futile is the law in the presence of so-called "misunderstandings".

Some resent cancer education which brings three or more persons to a physician without cancer for every one with it. Hysteria, they cry. Nonsense! It is not fact but fiction on which hysteria is based. Then there is the whole brawl of divergent opinion in regard to tonsillectomy, the importance of care of the deciduous teeth, and a hundred and one other matters. There are even physicians who advise against pasteurized milk! I sometimes think that certain members of the medical profession have delayed increasing the safety of our milk supply more than any other group.

I have, of course, selected instances ruthlessly to over-emphasize my point. On the other hand, I could give examples of the practitioner with a profound sense of community responsibility, who has made his peace with Hippocrates and his oath, and who deserves to be known as a health officer in his community far more than the individual who may strut fatuously under the title, devoting his life to fumigation, tin cans and ashes. But that is the other side of the shield.

We must get to the question of "Can or will the internist practice preventive medicine?" To answer this we must have definitions. What is an internist? I have nothing profound to contribute here. But it would seem to me that the internist, while making use of all the advances and complexities of medical knowledge, is the direct descendant of what suffering mankind so cherished and has now largely lost, the family physician at his best. He individualizes his advice not to the organ involved but to the whole patient, mental and physical, and to his family and his whole environment. To do that wisely in all instances would make Solomon hang his head!

What, on the other hand, is the practice of preventive medicine? Some lay people confuse it with birth control. We know the diseases against which we have effective prophylaxes, and others will be added unto them. We know how some diseases are spread and should not keep it as the secret of the Sphinx. We know something of the conditions that menace the pregnant woman, the infant, child, youth and adult; such as foci of infection, extreme deviation in weight, preposterous hygienic habits, and improper bodily mechanics. There is, of course, much more that we do not know. What are the extremes of the physiological normal in blood pressure, temperature, albuminuria, serology, diet, and the like? How far from normal must the person be in order to warrant his visiting a doctor without a suspicion of hysteria? The dentists say he should come regularly irrespective of pathology. The enthusiasts for health examinations say the same.

But for the effective health examination we must have a public which knows how to use such an examination. A despairing physician told me of an enraged woman whom he had

examined healthily. On vague suspicions in the chest he called for an X-ray. With delight he informed her that it was negative. In no uncertain terms she told him of her opinion of him for putting her to the unnecessary expense. She was in the dark ages when it was considered an admission of weakness if a doctor was ever seen reading a medical book. The doctor on his side was through with health examinations until the public was educated as to what to expect. Again, an enraged man said that all he got out of his examination was advice as to tonsillectomy. When asked if that wasn't good advice, he said he supposed so but that he didn't need to pay for it again as three other doctors had told him the same thing. Of course, such people are lazy. They look for the miracle, the self-reducing soap. They expect from the health examination the effortless road to eternal youth. No fee is too high for the physician to charge who must suffer with them. They need mental dynamite.

But even for the intelligent public do we know enough about these things at present to keep the sincere doctor on the one hand from being a back-slapper and on the other from being a crepe hanger? Won't we lose more than we gain by rushing in without complete knowledge? Is not ignorance the basic reason why the magnificent potential inherent in examinations of the supposedly well has been so little realized? In large part. But if ignorance forbade medical practice, how many physicians would handle pneumonia, arthritis, undulant fever, the common cold, in fact, any condition to which flesh is heir. Such a philosophy would prohibit efforts to save 30 per cent of the cancerous, to still further reduce tuberculosis from its place as the most killing disease in the ages fifteen to thirty-nine, to save mothers and babies throughout the country. Ignorance is no valid excuse for not using what we know. The temper of the public and the dignity and responsibility of the profession demand that the internist practice preventive medicine as we know it. He can, but in how many instances will he?

A Statistical Study Of The Coincidence Of Malignancy And Tuberculosis

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THE existence of a correlation, positive or negative, between any two major diseases is a subject which intrigues the mind of physician, statistician, biologist and layman. Two such fatal diseases as tuberculosis and malignancy have offered for many years a natural field for research and for speculation; and the literature abounds with case reports, statistical analyses and opinions as to the balance which the writer thinks to exist between these two conditions. A recent (and in fact the first thorough and statistically adequate) study of a large body of carefully prepared material is that of Pearl,[1] who concludes that "there is a definite and marked incompatibility or antagonism between the two diseases, cancer and tuberculosis, of such a sort that both occur together at the same time in florid activity in the same individual only with great rarity." It is the purpose of this paper to consider statistically the autopsy material from the Department of Pathology of the University of Michigan, and to analyze these statistics with a view to ascertaining any possible interrelationship of malignancy and tuberculosis. The statistical method has been essentially that of Pearl; but the conclusions drawn from the analysis do not support his statement quoted above.

No attempt will be made to review the history of this problem previous to Pearl's study. This phase of the subject is thoroughly discussed by him and a very complete bibliography will be found attached to his paper (loc. cit.). Most of the writers have taken as a starting point Rokitansky's[2] dictum, based not on statistical information but rather on his own experience, that cancer and tuberculosis very seldom occur together either in the same organ or the same individual. They have then, on the basis of their experience, set out to disagree with or substitute this doctrine. The statistical analyses previous to Pearl's are not fully adequate, either from the point of view of the material or of the manner of treatment. The literature since this time consists of clinical case reports of combined tuberculosis and carcinoma by Ainto,[3] Klink,[4] Callahan, Schiltz and Hellwig,[5] and Graham[6]. In addition to these case reports there has appeared an experimental study by Cherry[7] and a statistical review by Carlson and Bell.[8] Further reference will be made to these two papers.

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As already indicated, investigation of this problem has proceeded along three lines,—case reports, experimental investigations and statistical studies. Evidence based on the close association or lack of association of tuberculosis and malignancy in the same organ, while interesting, is contradictory and unconvincing. It has been held that certain organs, such as the ileum, where tuberculosis is common, relatively rarely show cancer, and on the other hand in the stomach, where cancer is often localized, tuberculosis is rare. Over against this observation are the numerous reports in the literature describing the close association of cancer and active tuberculosis in the same organ. It is impossible to draw any definite conclusions from such evidence.

Experimental work has followed two courses,—animal experimentation and the use of tuberculin in treating advanced cases of malignancy. As mentioned by Carlson and Bell (loc. cit.), the work on animals has not given uniform results. In 1926 Centanni and Rezzesi[9] injected mice (a type resistant to tuberculosis) with a transplantable adenocarcinoma. They found that live tubercle bacilli prevented tumor growth, tuberculin retarded it and dead tubercle bacilli had very little effect. Injecting tubercle bacilli directly into a tumor already present caused partial destruction, a result which can be produced also by injection of other toxic substances. When tumor and tubercle bacilli were injected in different parts of the body, the tumor growth was at first inhibited and then as the tumor developed the tuberculosis regressed. When neoplasm was injected into an animal previously infected with tuberculosis, the neoplasm grew more slowly. They attributed their results to an allergic reaction against neoplasm, caused by the tubercle bacilli.

Cherry[7] in 1929 studied spontaneous neoplasms occurring in a tuberculosis-resistant strain of mice. He inoculated these mice with living tubercle bacilli and found that neoplasms occurred spontaneously much more commonly in the inoculated mice than in those not inoculated. He states that he recovered acid-fast bacilli from 10% of his inoculated mice, but he does not state how many of these mice showed tumors. Three tuberculomas occurred, and in the protocols of these mice no mention is made of any neoplasms. It is not clear just how many of the mice of the inoculated series, which showed the high incidence of neoplasm, actually had an active tuberculosis.

The published reports on the use of tuberculin in the treatment of cancer have come from the Johns Hopkins Institute for Biological Research. Only cases which were hopeless from a surgical standpoint were considered as suitable material, and hence the field was scarcely favorable for good results. The last publication, a preliminary progress report by Pearl, Sutton and Howard,[10] gives six case histories. Four of these showed definite clinical improvement at the time of the report, one had died, and the other one showed serious symptoms from brain metastases. This does not necessarily have any bearing on the relationship of active tuberculosis to

cancer. In the use of tuberculin, one is dealing with a toxic substance which happens to be a bouillon filtrate of a culture of tubercle bacilli. Even though tuberculin should be found a valuable instrument in fighting cancer, it is not proven that the disease tuberculosis inhibits malignancy.

In preparing the statistical material for this paper, the entire series of autopsy protocols of the Department of Pathology of the University of Michigan was studied. All cases in which a complete examination of the trunk had not been allowed, cases in which microscopic examination was not complete, and those in which the age, sex and race were not recorded, were eliminated. From those remaining, there were isolated the cases of malignancy. Each of these cases was then controlled by the next case, not a malignancy, following it in the autopsy series, falling within five years of the age, of the same sex and of the same race (white or colored). This treatment is essentially that used by Pearl in his analysis, q.v. The only exception to this procedure was at the end of the series where those cases which could not be controlled by one later in the series, were controlled by the nearest one preceding which met the above conditions and which had not been already used. In this way cases in the cancer and control series are made comparable in time, thus eliminating errors arising from changing criteria or changing disease incidence; the possible error from the fact that malignancy is a disease primarily of later life than tuberculosis is eliminated, and sex and racial differences are equalized. A total of 514 cases of malignancy was used and 514 controls were set up in this manner.

In considering the coincidence of tuberculosis in both the cancer and control series a distinction is drawn between active and healed tuberculosis. The simple presence of caseation is not taken as evidence of activity, because it seems that a well encapsulated area of caseation is no more active than an area of calcification. A lesion is not considered active unless tuberculous granulation tissue has been found microscopically and there was evidence of proliferation or spread of the disease process.

It is frankly recognized that in the diagnosis of healed tuberculosis much depends on the criteria used and the thoroughness with which the prosector searched for evidence of the disease. However, since the control and malignancy cases are comparable in time, and since all cases used come from the autopsy service of one man, Dr. A. S. Warthin, these variables should equalize each other in the two series. The only evidence accepted as indicating healed tuberculosis is the finding of healed tubercles, such criteria as apical scarring and apical adhesions being discarded as not uniformly diagnostic of tuberculosis.

The cases which were selected in this manner were tabulated, noting in each instance the major condition which was responsible for the individual's death. A summary of the results obtained is given in Table 1.

The results were further analyzed as to sex with the results given in table 2. Less than 1% of the cases in the total series are of the colored

race, so that this factor was discarded in analyzing the statistics.

TABLE I

Malignancy Series—514 cases		
Active tuberculosis	27 cases	5.3%
Healed tuberculosis	126 cases	24.5%
Control Series—514 cases		
Active tuberculosis	58 cases	11.3%
Healed tuberculosis	150 cases	29.2%

TABLE 2

Malignancy Series		
Males	367 cases	
Active tuberculosis	20 cases	5.4%
Healed tuberculosis	87 cases	23.7%
Females	147 cases	
Active tuberculosis	7 cases	4.8%
Healed tuberculosis	39 cases	26.5%
Control Series		
Males	367 cases	
Active tuberculosis	47 cases	12.8%
Healed tuberculosis	114 cases	31.1%
Females	147 cases	
Active tuberculosis	11 cases	7.5%
Healed tuberculosis	36 cases	24.5%

It will be seen that while there is very little difference in the incidence of healed tuberculosis between the malignancy and control groups, the active tuberculosis, both in the total series and in the segregation by sexes, is practically twice as great in the non-cancerous group as in those showing some form of malignancy. These results are in close agreement with those found by Pearl and also by Carlson and Bell (loc. cit.). In Pearl's total series active tuberculosis was found in 6.6% of the malignant cases and 16.3% of the non-malignant cases. Healed tuberculosis occurred in 28.1% of the cancerous cases and 26.7% of the control cases. Carlson and Bell found also an equal incidence of healed tuberculosis in the two series, but active tuberculosis was much more common in the non-cancerous controls than in those showing some form of malignancy. The method used by Carlson and Bell differs from that used by Pearl and in this paper. They do not consider the sexes separately, and they have charted their cases by decades, taking the percentage of tuberculosis in all post mortems, and in cancer cases falling in that age span. The close parallelism between the three series, taken from different sections of the country and using two such different statistical methods lends weight to the results obtained. It may be safely said that active tuberculosis is much more common in non-cancerous individuals than in those with some form of malignancy, while healed tuberculosis occurs in about equal frequency in both groups, if the comparison is made using as controls those who die from all causes except malignancy,—including among these diseases tuberculosis itself.

As already pointed out by Carlson and Bell[8] there is an important objection to the use of a group as controls in which all manner of diseases were fundamental in causing death. They have demonstrated that a similar apparent antagonism can be demonstrated between heart disease and malignancy, and between heart disease and tuberculosis. In my series of 514 cancer cases, practically all died as a direct result of the malignant condition, and in only 3 instances was death due to tuberculosis. In the control group, on the other hand, 34 of the cases of active tuberculosis died as a result of

their tuberculosis. The question arises as to how many of these cases might have developed cancer had they not died first of tuberculosis. Since the cancer and control series obtained are not entirely comparable, it therefore seems that the results which are tabulated above are misleading.

It does not, however, seem impossible to set up a series of malignancy and control cases which are more nearly comparable. In 24 of the 27, or 88.9% of the cases of active tuberculosis found associated with cancer, the tuberculosis was a secondary factor and not the condition leading to the individual's death. In setting up the new series for comparison the three cases dying of tuberculosis were excluded leaving a total of 511 cases of malignant disease. Similarly the 34 cases from the control series in which the individual died of tuberculosis were excluded. These vacancies were filled in by taking the next following protocol in the autopsy series, not already used as a control, which met the conditions already outlined for selecting controls (q.v.). This gives two series in which active tuberculosis, if present is not the primary, underlying cause of death. It was found that in the new controls taken three cases of active tuberculosis occurred with death due to some other factor, and these, of course, are added to the total cases of active tuberculosis in the control series. A summary of this new comparison is given in table 3.

It is evident that there is no significant variation in the percentage results in the cancer and control series as given above. The position is taken that these results more nearly represent an answer to the problem of whether tuberculosis and cancer are associated more often, or less often than tuberculosis and any other disease capable of causing death. In the series summarized in tables 1 and 2 tuberculosis combined with cancer was being compared with tuberculosis, —sometimes combined with some other major disease and sometimes the only serious condition from which the individual was suffering. Such a comparison is obviously apt to lead into error. In the series summarized in table 3, on the other hand, the tuberculosis is in every instance, in both cancer and control series, combined with another serious condition, and in fact with another disease which caused the death. This gives a cancer series and a control series which are comparable, and from a study of which it is impossible to demonstrate any correlation, positive or negative, between active tuberculosis and cancer.

TABLE 3

Malignancy Series .....511 cases		
Active tuberculosis	24 cases....	4.7%
Control Series .....511 cases		
Active tuberculosis	27 cases....	5.3%
DISTRIBUTION AS TO SEXES		
Malignancy Series		
Males .....366 cases		
Active tuberculosis	19 cases....	5.2%
Females .....145 cases		
Active tuberculosis	5 cases....	3.4%
Control Series		
Males .....366 cases		
Active tuberculosis	21 cases....	5.7%
Females .....145 cases		
Active tuberculosis	6 cases....	4.1%

The evidence from case reports, experimental work and statistics fails to establish any convincing relationship between these two diseases. The

fact that healed tuberculosis is found with equal frequency in cancerous and non-cancerous individuals shows that a past infection is without bearing on the development of malignancy. The position that the person with active tuberculosis is less apt to have a malignancy, because of an immunity to cancer, can not be substantiated by the statistics presented in this paper. He is less apt to have cancer because he may die of his tuberculosis before he reaches the age at which cancer is most common. The occurrence together of the two diseases appears to follow closely the occurrence of tuberculosis with other serious diseases capable of causing death.

Summary

1. Investigation of the concomitant occurrence of cancer and tuberculosis by means of case studies yields many interesting reports but no valid evidence of the frequency of the combined diseases.

2. The results from animal experimentation are contradictory and inconclusive.

3. The result obtained, or the lack thereof, in the treatment of cancer by tuberculin does not bear directly on the relationship of the two diseases, for the effect of the tuberculin may be due to the fact that it is a toxic substance and not to its derivation from the tubercle bacillus.

4. Statistical studies have been inadequate until recently, and the two most recent and best disagree in their conclusions.

5. Statistical analysis of the autopsy records of the Department of Pathology of the University of Michigan, when properly controlled, shows that active tuberculosis occurs neither more nor less frequently combined with malignancy than it does combined with any other major disease capable of producing death. Healed tuberculosis occurs with approximately equal frequency in cancerous and non-cancerous individuals.

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Editorials

CANCER AND TUBERCULOSIS

The view that there is an antagonism between cancer and tuberculosis is probably due chiefly to the teachings of Rokitansky, who wholly on the grounds of an extensive gross pathological experience concluded that there was a definite antagonism between active, florid tuberculosis and cancer. He especially emphasized the fact that cancer is only rarely found at those sites where tuberculosis most frequently occurs, as the lungs, for example; and that conversely the most favorite sites of cancer as, for example, the esophagus, stomach, rectum and ovary, are only rarely the seat of tuberculosis. An extensive literature on this subject has followed Rokitansky, made up largely of reports of cases in which there was a coincidental tuberculosis and carcinoma, and numerous recent papers of this kind have appeared. Rokitansky's dictum has had the effect of stimulating pathologists to such reports of the coexistence of the two diseases. Statistical studies of autopsy material have also been frequently carried out with respect to this question, and the majority of these have decided in favor of the Rokitansky view of the infrequent coincidence of the two diseases in the same individual. Some of these studies advance the view that the disposition to cancer carries along with it a high resistance to infection in general, not only to tuberculosis, but also to syphilis, malaria and leprosy. On the other hand a familial association of tuberculosis and cancer has been noted by several writers, but these observations are rejected by Pearl as being the result of inadequate statistical technique. The latter considers the evidence as set forth in the literature to be "conclusive, to an overwhelming degree, to the effect that florid active tuberculosis and cancer occur together only with the greatest rarity." As to the experimental evidence favoring this view, such is extremely meager, and consists chiefly in the altogether inadequate experiments of Centanni and Rezzesi. These investigators worked with a strain of mice highly resistant to infection with the tubercle bacillus, and a transplantable adenocarcinoma which had a virulence of about 100 per cent. Injection of a mixture of cancer cells and living tubercle bacilli produced no tumors. Simultaneous injections of these two materials separately in different parts of the body depressed the rate of development of the neoplasm, though in some cases only temporarily. Previous infection of the animals with tubercle bacilli delayed the development of the subsequently inoculated tumor. Injection of the bacilli into an already growing tumor partially destroyed it, but some of the animals died with toxic symptoms. Dead tubercle bacilli had no influence in parallel experiments. Tuberculin mixed with the

tumor emulsion retarded or inhibited growth. They attributed their results to an allergic reaction against neoplasm, caused by the tubercle bacilli. Directly opposed to the observations made by Centanni and Rezzesi is the experimental work of Cherry (1929) who studied the development of spontaneous neoplasms occurring in a tuberculosis-resistant strain of mice. In such mice inoculated with living tubercle bacilli, he found that neoplasms occurred spontaneously much more frequently than in those not inoculated. On the grounds of a statistical study of 816 autopsies on patients having malignant tumors in the Johns Hopkins Hospital, and a case-for-case control series not having cancer or any other malignant tumor, Raymond Pearl found that active tuberculous lesions were found at autopsy in only 6.6 per cent of 816 persons with malignant growths, and in 16.3 per cent of 816 persons without malignant tumors. In 886 persons with active florid tuberculosis there were but 11 cases of malignant tumors, or 1.2 per cent of the total number. On the other hand, in 886 persons with no recorded tuberculous lesions at autopsy, of the same age, sex and racial distribution, there were 82 cases of malignant tumors, or 9.3 per cent. On the basis of these findings, Pearl concludes that there is a definite and marked incompatibility or antagonism between the two diseases, cancer and tuberculosis, of such sort that both occur together at the same time in florid activity in the same individual only with great rarity. This conclusion would not have been so bad, and would have passed only for an interesting statistical excursion of the usual degree of value, had not Pearl been bitten by the flea of therapeutic application of these statistical results, as to the treatment of malignant tumors in human beings wih some form of tuberculin. In connection with Sutton such treatment has actually been undertaken, with the following statement, as to results: "All that can be said at the present time is that in the cases treated the longest the tumors have shown definite retrogression. And the general condition of these patients is sufficiently encouraging to warrant our continuing the work, but a long time must pass before any final report can be made." A serious matter this, of arousing, even in the slightest degree, futile hopes of a possible cancer cure, in the many unhappy victims of malignancy, only too eager to grasp at any straw in the way of therapy. Futile—because of the lack of any positive evidence that such treatment will do anything more than to cause a possible temporary regression of the older parts of the neoplasm, produced not through any biologic antagonism between the two diseases, or the result of any constitutional differences, but wholly through the toxic action of the tuberculin, an effect comparable to that produced by the Coley's mixture of toxins—and nothing more than that. Further, Pearl is hoisted by his own petard of "inadequate statistical technique." Carlson and Bell in reporting a study of autopsy material similar to that of Pearl, found also that active tuberculosis was more common in the non-cancerous individuals than in those with some form of malignancy, while healed tuberculosis occurs with about equal frequency in both groups. But as

Carlson and Bell point out there is a serious objection to the use of a group as controls in which all manner of diseases were instrumental in causing death. They have demonstrated that a similar apparent antagonism can be demonstrated between heart disease and malignancy, and between heart disease and tuberculosis. And for that matter between tuberculosis and deaths from automobile accidents! Further, Fortune in this issue, gives another statistical study of the association of tuberculosis and cancer, using a somewhat different method of control, as reference to his paper will show. The evidence from his statistical study likewise fails to establish the existence of any positive antagonism between the two diseases. The fact that healed tuberculosis is found with equal frequency in cancerous and non-cancerous individuals shows that a past infection is without any bearing on the development of malignancy. The statistics presented by both Carlson and Bell, and Fortune do not offer any support to the view that the person with active tuberculosis is less apt to have a malignancy, because of an immunity to cancer. He is less apt to have cancer, only because he usually dies of his tuberculosis before he reaches the cancer age. The coincident occurrence of the two diseases appears to follow closely the coincident occurrence of tuberculosis with other serious diseases capable of causing death. Active tuberculosis occurs neither more nor less frequently combined with malignancy than it does with any other major disease capable of producing death. Healed tuberculosis occurs with equal frequency in cancerous and non-cancerous individuals. Pearl would have been more fortunate had he developed Beneke's conception of constitutional differences between those predisposed to malignant disease and those predisposed to tuberculosis. That there exist a heredo-neoplasia constitution and a heredo-tuberculosis constitution there can be but little doubt. The patient with the latter will usually succumb to his constitutional fate before reaching the carcinoma age. There is no reason why a hybrid of these two constitutions may not exist in the same individual; and there is abundant evidence to prove that such do occur. The existence of special constitutional susceptibilities to the two diseases does not mean that any biologic antagonism exists between the two processes. There appears to be, on the other hand, some evidence for the existence of a definite familial relationship between the two diseases. In certain families showing a family susceptibility to cancer in those who live to the cancer age, a very high mortality of the younger members of the given family from tuberculosis has been repeatedly observed. Whether there be any positive relationship of the susceptibilities of the two diseases to each other, as may hereby be indicated, the general fact remains, in explanation of the autopsy infrequency of their coincidental association, that the tuberculous die young, before attaining the age of malignancy.

Abstracts

The Epileptic Seizure. Its Relation to Normal Thought and Action. By Joshua Rosett (Archives of Neurology and Psychiatry, April, 1929, p. 731).

That epilepsy is a symptom-complex incidental to an abnormal functioning of the brain is an opinon advanced some thousands of years ago by Hippocrates; and from this opinion few, if any, dissent today. The discovery, however, of a large number of abnormal conditions, which by their action on the brain, may give rise to the disorder, compels a point of view from which the truth of the general proposition is seen in a new light. Every physician is impressed with the fact that out of a number of persons who have been subject to the same disease or accident, only a few become afflicted with epilepsy. Observations by Wilson, Hanptmann, Wallon and others, on the relation of war injuries to the causation of epilepsy, reveal the existence of predisposing factors in a large number of cases. The assumption that a disease or accident is potent in producing the disorder only when acting on an abnormal brain is indeed upheld by the study of its hereditary features. The latter, however, may be variously interpreted. Gowers' statistics, showing that a large proportion of epileptic patients are born of insane or epileptic antecedents, are upheld by the latest investigations. But all such statistics fail to give any information as to the nature of the particular defect in the parent which, when inherited by the child, makes the latter an epileptic. Thus, when one finds that of two persons who have received an equally heavy blow on the head, the one who in consequence became afflicted with epilepsy or insanity was the child of an insane or epileptic parent, we are still in ignorance as to whether the underlying cause of the disorder in both parent and child was due to some constitutional defect acting on a normal brain, or to an essentially abnormal brain. Much light is shed on this difficult problem by certain discoveries. One is the discovery of the frequency of intra-ocular and meningeal hemorrhages in the new born; and the second is the growing importance of metabolic disorders as a factor in epilepsy. Their significance of the deepest gloom is mitigated by their value as a warning of impending danger to the human race. There is strong probability that all neuro-heredity statistics, including those of epilepsy, are in a way misleading. It is impossible to prove the inheritance of a defective nervous system as such; generation after generation may be in possession of a defect consisting not only of a disproportion between the child's head and the mother's pelvis and pelvic organs, but of a defective correspondence between the special metabolism of pregnancy and the embryonic formation of the enormously complicated structure of the human brain. Even when epilepsy is apparently inherited from the father, it is unsafe to conclude that there is an inheritance of a defective brain rather than an inheritance consisting of a metabolic defect which by its action on the brain is the cause of epilepsy in both father and child. That the arts of obstetrics and gynecology are adequate to save a number of lives of both mothers and infants, and even to reduce the percentage of intracranial damage, is an established fact. But no rational person can doubt that these recently arrived arts must perpetuate defects by enabling defectives to survive and procreate. Whether the progress of the medical arts will outstrip and compensate for the increasing number of defectives in successive generations, or whether a point will be reached when the medical arts will be swamped by the number of defectives, only the future can show.

Epilepsy is a form of the tetanic state which has its origin in that normal inhibition of the sensory system which results in a release of muscular activity. The sensory and muscular manifestations of the epileptic seizure are not essentially different from the processes of normal thought and normal action. The feature which distinguishes the epileptic seizure from normal thought, imagery and muscular activity is an increased facility and generally a greater degree of nerve inhibition. If the wave of inhibition extends only a short distance along the sensory pathway and recedes before completely extinguishing the function of the association systems, then such a minor seizure is devoid of muscular manifestations. If the wave of inhibtion, in both the epileptic seizure and the process of thought, extinguishes all or a part of the highest portion of the sensory pathway—the association systems of the cerebrum—then the function of the efferent systems become manifest to a corresponding extent. The mechanisms of posture may be observed in the epileptic seizure to manifest their function before those of movement. The convulsive postures and movements of the epileptic, when reviewed in the prone position of the patient, appear to be irregular and absurd. Judged, however, as though the patient were in the upright position, they are unmistakably postures and movements which are integrated into normal patterns of muscular co-ordination. Outside of the occasional tremors and twitches which cannot be accounted for in the present state of knowledge, the movements are organized into complete and familiar acts which are frequently characterized by a considerable degree of beauty and grace. So varied are the acts of the convulsion in different individuals that it is not an exaggeration to say that there is hardly a normal posture-movement which is not represented in the convulsion of the unconscious epileptic. The various integrated movements of the epileptic convulsion, however, do not have reference to any co-ordinated acts which the person may have learned to execute in his conscious state. As a matter of fact, the convulsive acts are such as the conscious epileptic is unable to repeat on request. The patterns of the co-ordinated movements and postures of the convulsion must, therefore, be inherent in the person's nervous system. Since the almost infinitely varied acts of the convulsion are not essentially different from normally integrated movements and postures, one may conclude that in normal persons the patterns of posture and movement which are integrated into discernibly separate acts are inherent in the nervous system. Other things being equal, the ultimate success or failure of a course of training in the execution of any skilled act must, therefore, depend on whether the particular posture-movement patterns exist or do not exist in the nervous system of the particular person. The detailed records of the various stages of the epileptic seizure show that the more profound the inhibition of the sensory system, the greater is the strength of the muscular contractions. The conclusion is therefore justified that a given degree of muscular contraction is normally conditioned by a corresponding degree of sensory inhibition. In the cases observed in this study, no change of a given posture-movement pattern could be produced by stimulation of the peripheral receptors. The amount of afferent nerve function remaining in the unconscious epileptic patient during the convulsion must therefore be less than in the animal decerebrated by a section at the highest level of the midbrain. If the epileptic seizure is a form of the tetanic state which is distinguished from normal processes of thought and action merely by an increased facility of inhibition of the nerve pathways, then it must be subject to the same laws of training to which normal mental and muscular function is subject. Experiments on animals show that a tolerance for the tetanic state can be acquired by training, even when the defect is as definite as the want of parathyroid influence. That an increased tolerance for the tetanic state can be acquired by a certain course of training in human beings is also shown by the experiments on epileptic patients in connection with the present work. Although the method employed in these experiments is,

on account of its great difficulty, impractical as a treatment for epilepsy, it is nevertheless suggestive of a certain line of education. The particular line to be pursued, however, must be left to the devices of the specialist.

A Tentative Classification of the Forms of Chronic Splenomegaly of Unknown or Uncertain Origin. By J. W. McNee (Glasgow Medical Journal, May, 1929, p. 288).

While at the present time no adequate clinical differentiation between the various forms of chronic splenomegaly is possible, a classification of an imperfect kind, based on differences in pathological anatomy and histology, has been attempted. The question of how far bacteriological methods may influence classification, and whether, for instance, aspergillum-like organisms are of etiological importance, is left open for further investigation. McNee's classification of chronic splenomegaly of unknown or uncertain origin is, as follows:

1. Splenomegaly with peri-ellipsoidal hæmorrhages and nodular siderosis (?? splenic mycosis).
2. Chronic hemolytic (acholuric) jaundice.
3. Thrombo-phlebitic splenomegaly.
4. Chronic splenic hypertrophy, with or without fibrosis.
5. Bantis' disease. *Rare.*
6. "Reticulo-endotheliosis" of the spleen.
   (a) slight (? chronic infections), or marked.
   (b) lipoidal group, diabetes, etc.
   (c) Gaucher-Pick-Niemann group.
   (d) tumors.
7. Undetermined group.
   (?) chronic aleukemic leukemia.
   (?) primary lymphadenoma of spleen, and others.

The history of our knowledge of the spleen and its diseases has been one of very slow development. One important fact going far back in the hisotry of medicine is the knowledge that this organ is not necessary to life. Its structure, especially the finer histological details, has been imperfectly known, and has recently been investigated anew. Old facts concerning the ellipsoids and the vascular arrangements of the organ have been brought again to notice and new interpretations placed on some of them. The physiology of the spleen has been investigated from new angles by Barcroft and his colleagues, and the fruits of this work have not yet been fully gathered. Some of the diseases of the organ, such as those due to the parasites of syphilis and malaria, are easily understood; while even in some general diseases of unknown etiology, such as lymphadenoma, the histological changes and chronic enlargement of the organ can be rationally explained. There has remained hitherto a large group of cases of splenomegaly of quite unknown or of uncertain origin to which for the moment the term chronic splenic anemia is perhaps most suitably applied. No clinical classification of these cases is yet possible, but an attempt has been made to separate into groups, on histological grounds, a very large series of spleens which have been available for examination. The rough and entirely tentative classification, as given above, has been made, the shortcomings of which are obvious, but which may serve as a basis on which to build.

Current Studies of Undulant Fever. By H. E. Hasseltine (Public Health Reports, July, 1929).

The first case of Malta fever in the United States was reported by Craig twenty-four years ago, who prophesied that a careful differential study of the obscure continued fevers prevalent in this country will result in the demonstration that Malta fever is by no means a rare disease in the warmer portions of the United States, and that many of the so-called anomalous cases of typhoid fever are in reality instances of infection with the micro-organism of Malta fever. This was practically forgotten until the disease was recognized by Ferenbaugh and Gentry in the goat-raising sections of Texas; and even then it was considered only of passing interest. In 1917 Evans called attention ot the fact that the organism causing Malta fever was practically identical with that causing infectious abortion of cattle; and in 1924, Keefer reported a case of Malta fever in man which was proved by

positive blood culture to be due to the abortus organism. Since 1926, each year has brought an increasing number of reported cases. As to the amount of undulant fever in the United States there are no reliable statistics. Information collected up to January 1, 1929, showed that 40 States reported 560 positive agglutination tests in 1928, 18 States reported 194 positive in 1927, and in 1926, 7 States reported 34 positive. Over 300 clinical cases of the infection have been reported in the literature since January 1, 1927. It is not known how many cases have passed unrecognized, or recognized and not reported. Among the diseases that may be confused with undulant fever are typhoid and paratyphoid fever, tuberculosis, rheumatism, malaria, influenza, focal infections, sinusitis, appendicitis and tularemia. The first symptom usually is a general feeling of weakness in the afternoon, accompanied by headache, or general aching. The patient then discovers that he has fever, which is usually preceded by chilliness, or a definite rigor, followed by a hot stage and a rather profuse perspiration, particularly noticeable upon awakening. When questioned closely, most patients report that the sweating is limited to the upper half of the body. It is quite common for patients to feel so well in the morning that they want to go to work; but if they do, they are ready to quit early in the afternoon. When seen in the febrile stage the patient appears only slightly ill, and if his temperature is taken, it will be surprising to find it 1-3 degrees higher than the general appearance of the patient would indicate. The daily variation is usually marked, being at or near normal in the morning, and going to 102° or 104° in the afternoon. If taken every four hours, a rather irregular curve within the day is frequently noted. The blood picture usually shows a slight anemia, a slight leucopenia and a considerable increase in the lymphocytes, with a corresponding reduction of the polynuclears. After the fever has risen by irregular steps to a maximum of 103-104°, occasionally higher, it usually declines by lysis, and remains normal for a period varying from three days upward. Then another febrile wave begins, usually not quite so severe, nor quite as long as the first, followed by an afebrile wave slightly longer than the first. Some cases have but one febrile wave, others have them irregularly over a period of one to three years. The general symptoms of the disease come and go with the febrile wave. Joint pains, especially upon getting about after the fever has returned to normal, are present in most cases. They vary from slight pain to moderate interference with the function of the joints. Anorexia, constipation, insomnia and increased irritability are present in a majority of cases. The most prominent complications reported have been orchitis or epididymitis, and abdominal conditions, caused by a localization of the infection in the viscera, particularly in the female reproductive organs. Prostatic symptoms have been noted in the male, and abortion in pregnant women has been attributed frequently to this infection. It is too early to know whether the infection may cause any later sequelae, such as sterility, which the disease is known to cause in some of the domestic animals that it attacks. Comparatively little is known of the pathology of the infection in human beings. Whether the infection with the types of *Brucella abortus* differs in its pathology from that of *Brucella melitensis* is not yet known. For diagnosis, blood serum should be submitted for an agglutination test against Brucella abortus as well as against the typhoid organism. A positive aggultination test in 1:80 dilution, or higher, in a case presenting the symptoms of undulant fever warrants a diagnosis even in the absence of positive blood cultures. The obtaining of blood cultures is important in order that the strain of the infecting organism may be determined. At the present time, it appears that there are at least three strains of the Brucella germs that may cause undulant fever, the caprine, bovine, and porcine strains. The exact relationship of these strains to human undulant fever remains to be determined.

Reviews

Recent Advances in Cardiology. By G. F. Terence East, M.A. (Oxon.), F.R.C.P. (Lond.), Junior Physician, King's College Hospital; Physician, Woolwich Memorial Hospital; Sometime Radcliffe Travelling Fellow, University College, Oxford; and G. W. Curtis Bain, M.C., M.B. (Oxon.), M.R.C.P. (Lond.), Assistant Physician, Harrogate Infirmary. 342 pages, 12 plates and 57 text-figures. P. Blakiston's Son & Co., Philadelphia, 1929. Price in cloth, $3.50.

This volume is one of the "Recent Advance Series," and attempts to give a summary of the new knowledge of the last twenty-five years regarding the heart and circulation. It makes an appeal, both to the older practitioner who wishes to become conversant with the latest ideas, and also to those who seek special knowledge upon cardiac subjects. It, therefore, embraces both the practical and academic aspects of cardiology. Throughout the book the electrocvardiogram has been considered as part of the clinical picture. The majority of the references are to work of the last decade. While in a book so limited in size adequate abstracts of the work referred to cannot be given, the book still covers the ground of modern cardiology very thoroughly. Few important modern contributions to this subject have been missed. The electrocardiographic illustrations are very good. The book is well printed, and the material and discussions are very good. It will be useful to the general internist as well as to the specialist in cardiology.

Sterilization for Human Betterment. By E. S. Gosney, B.S., L.L.B., and Paul Popenoe, D.Sc. 202 pages. The MacMillan Company, New York, 1929. Price in cloth, $2.00.

This is a publication of the Human Betterment Foundation; and gives a summary of 6,255 operations for sterilization performed in California, 1909-1929. There were 601 more males than females sterilized, 1,488 were on feeble-minded, and in this group there were 330 more females than males. All feeble-minded patients are now sterilized before they are allowed to leave the state home at Sonoma. One in twelve of all the insane admitted to the state hospitals since the law was passed has been sterilized. One in five or six of the new admissions is now sterilized. Sterilization is done only w' ere there is danger of defective children. This book reviews the effects of the operation as carried out in California, and gives a general discussion of the various aspects of the problem. It is written in popular language, and in a clear simple style. It is an excellent presentation of the subject from all standpoints, and should be read by all thinking citizens. The chapters on "Sterilization for Social Reasons" and for "Eugenic Reasons" are particularly useful to the ordinary reader in helping him to formulate his opinions as to the justification of sterilization. The general text is followed by a number of valuable appendices. This book cannot help but clarify the subject in the minds of all who read it; and this is a manner upon which all thoughtful citizens, medical as well as lay, should be fully informed.

An Introduction to the Study of Physic [Now for the First Time Published]. By William Heberden [1710-1801]. A Prefatory Essay by LeRoy Crummer. With a Reprint of Heberden's "Some Account of a Disorder of the Breast." 159 pages, portrait in photogravure, 6 illustrations. Paul B. Hoeber, Inc., New York, 1929. Price in cloth, $2.00.

This unpublished original manuscript of Heberden was a lucky find by Dr. Crummer

in a little second-hand book shop in the south of London. Picked up as a medical manuscript in Wales the week before by the book-seller, the volume handed to Dr. Crummer had written on the title-page "An Introduction to the Study of Physic," and beneath this the signature "William Heberden." We may be sure that this was an exciting moment in the book-collector's life, and he tells us that when he left the shop the manuscripts were safely under his arm. Then followed the excitement of identifying the signature as being actually Heberden's, and of the discovery that the manuscript represented a hitherto unpublished work of Heberden. All of this is told by the author in a most interesting manner calculated to excite an answering thrill in all other collectors who may read this prefatory essay. When compared with the manuscript of Heberden's "Commentarii" in the Royal College of Physicians, the manuscripts found by Dr. Crummer proved to be identical with the former in paper, quire arrangement, format and the limp vellum binding, as well as in the beautiful script of William Heberden. In one of the volumes found there is written on the recto of seventy-four pages the manuscript of "An Introduction to the Study of Physic." There is no date recorded in the manuscript, nor any direct citation of current events which would definitely place the year or years of its composition. Crummer thinks that it must have been written in the latter part of Heberden's Cambridge period, or at least in the early years of his life in London (1744-1755). He thinks it fair to assume that the original idea was formed while he was teaching at Cambridge, that the material was finally revised during his early years in London, and that the final form represents Heberden's plan for a proper arrangement of the medical curriculum at the end of his experience in teaching in Cambridge. This period was a very significant one in the history of English medicine. A general dissatisfaction in medical education was manifest in different quarters. Edinburgh was just beginning its brilliant career as a primary center of medical education. Written at such a period the "Introduction" may be regarded from two standpoints, the purely personal and the other, as an exhibit hitherto unrecorded in the general history of medical education. It would seem that in the "Introduction" Heberden has given an autobiographic survey of his own method of study, a list of the authorities in his judgment most worth while, and a criticism of antecedent medical literature based on an unequaled understanding of original texts. His comments on the latter became authoritative, as from one who had a complete understanding of the state of the medical sciences of the time, as well as an extraordinary ability in the languages used in the originals. The test of time has to ? great mesure justified his choice of authorities. He mentions one hundred and fourteen books. He insisted upon the importance of studying source literature; his chapter on anatomy with few changes would hold its place in one of the great educational arguments of the present time. Had Heberden elaborated the ideas expressed in this manuscript, medical education might have been advanced a full century. The manuscript has been printed without change or emendation. The volume closes with a reprint of Heberden's "On a Disorder of the Breast," the classic report on Angina Pectoris. The book is beautifully printed, and is to be counted as another of Hoeber's successful achievements in medical history publication. It should be in every one's collection.

Applied Electrocardiography. By A. E. Parsonnet, M.D., F.A.C.P., Attending Physician and Cardiologist, Beth Israel Hospital, Newark, N.J.; and A. S. Hyman, A.B., M.D., F.A.C.P., Associate Physician and Cardiologist-in-Chief, Beth David Hospital, New York. With a Foreword by Harlow Brooks, M.D., F.A.C.P., Professor of Clinical Medicine, New York Univetrsity. 206 pages, 120 illustrations. The MacMillan Company, New York, 1929. Price in cloth, $4.00.

No mechanism of the entire mammalian make-up has aroused more speculative interest among phsiologists and anatomists than that of the heart. With each succeeding generation there has come out some new

device or method whereb greater knowledge of the heart's action could be obtained by the practicing physician. Thus have appeared in succession the stethoscope, blood-pressure apparatus, the art of percussion, the polygraph, and lastly the electrocardiograph; all serving to present to the physician new and better information in regard to the functional integrity of the cardiovascular system. So detailed and so complex has become the information about the heart, derived from these various methods of examination, that the physician today stands confused and perplexed when confronted with the problem of examining the heart at the bedside. The authors recognize full well the apprehensive attitude displayed by most physicians at the mere mention of the word electrocardiogram; and it is their hope that this volume may dispel that inferiority complex that surrounds the physician when contemplating the use of the electrocardiograph. This book is written for those practitioners who have neither the time nor the scientific make-up needed for a thorough perusal and contemplation of the extensive literature on electrocardiography. An attempt is made in it to reduce the knowledge amassed by the pioneer investigators in this field to simple truths, essential in the every day experience of the practicing physician. No apology is made for the attempt to present problems of the utmost scientific abstractness in terms of bedside simplicity. Highly problematical and debatable hypotheses are omitted. Free use is made, however, of the established phraseology of the cardiologic laboratory in the belief that the terms employed to describe electrocardiographic findings will soon become an integral and familiar part of the physician's vocabulary. The authors have selected typical graphic records of the common diseases of the heart, and have taken advantage of their rich supply of records obtained from thousands of cases. The theory and application of electrocardiographic technique has been so simplified that the interpretation of graphic heart records is made easily available to every practitioner of medicine. The book is designed for the education of the practitioner in the art of interpreting the clinical features of his cases. It is a book written by clinicians for clinicians rather than by physiologists or technicians. In this respect it fills a definite need.

Otosclerosis. A Resumé of the Literature to July, 1928. Compiled under the Direction of the Committee on Otosclerosis, American Otological Society; Nowal H. Pierce, M.D., Eugene A. Crockett, M.D., James F. McKernon, M.D., J. Gordon Wilson, M.D., J. Gordon Wilson, M.D., Arthur B. Duel, M.D., Editor. Volumes I and II. 684 pages with indices. Paul B. Hoeber, Inc., New York, 1929. Price in cloth, $15.00.

The Committee appointed by the American Otological Society, in 1925, undertook to make a complete resumé of the literature on Otosclerosis. These volumes present the results of this work. Any comment on, or criticism of, the subject matter has been purposely avoided. The resources of the largest libraries in the United States—the Surgeon-General's Library and the Library of the New York Academy of Medicine—have been used in the compilation of this work. Its chronological arrangement shows the development of our present knowledge and understanding of otosclerosis in all of its phases. Not only are the pathological findings of various investigators presented in detail, but also the numerous theories as to its etiology and the other phases of the snbject that are still open to discussion. No other such comprehensive survey of the literature on this subject has thus far been published. It shows what is actually known in regard to otosclerosis, and suggests the wide fields that are still open to scientific investigation and research. Here is presented a wealth of material which is otherwise available only in widely scattered form and places, in many different languages, and in many inaccessible journals. This volume brings to the otologist all the available data on otosclerosis in an easily usable form. Every otologist, whether research worker or practitioner, needs to be familiar with the survey, so that he may know what is, and what is not, established fact in regard to oto-

sclerosis, its pathology, etiology, diagnosis and treatment. This compilation was carried on as part of a program of research in otosclerosis which the American Otological Society began in 1926, under a grant of $90,000 made by the Carnegie Corporation. This subsidy, extending over a period of five years, was awarded in amounts decreasing each year, with the expectation that the Society could build up an independent fund to expound and carry on the work. A campaign to secure a permanent endowment fund of $2,500,000 is now under way. The Scientific Committee of the Otological Society plans first to investigate the chronic progressive types of the disease. Later the research will be extended to other otological problems. The contents of the two volumes are arranged as follows: Volume I, Preface; Section I, Pathology, Stapes Ankylosis, Changes in the Labyrinthine Capsule; Section II, Etiology, Heredity as an Etiological Factor, Congenital Conditions in the Labyrinthine Capsule, Influence of Local and General Conditions. Volume II, Section III, Symptoms and Diagnosis; Section IV, Treatment. There are appended full bibliographies and indices. No otologist can afford to be without these two volumes with their complete resumé of all our knowledge on this important subject.

College News Notes

THE MINNEAPOLIS SESSION of THE AMERICAN COLLEGE OF PHYSICIANS

S. Marx White, M.D., General Chairman of Arrangements

Preparations for the Minneapolis meeting of the College during the week of February 10th are well advanced. The program already under way has a character and content to lure every member, Fellow or Associate as the case may be, and to attract as well a great number who may be thinking of affiliation with the College or who may be interested only in the scientific material presented. Details of the Scientific Session and of the Clinics will be given in a later issue of the ANNALS. A glance meanwhile at the setting should be of interest.

Minneapolis lies, as the Mississippi River flows, about five hundred miles from the source of the Father of Waters, and nearly two thousand miles from its mouth in the Gulf of Mexico. It has been made, by vast engineering works, the head of navigation of this waterway and will soon be of even greater importance in the transportation system of the Valley and of the nation.

There was a time, not so long ago, when the waterway was the most important means of transportation to the inland empire centering here, and brought the famous voyageurs and missionaries to the neighborhood of St. Anthony Falls. Points of interest, avenues and institutions commemorate the names of Hennepin, Nicollet, Radisson and Marquette. Joliet, Groseilliers, La Ferriere and Le Sueur began their journeys of exploration here. Mendota, the site of Sibley House, the first house built in the territory, lies about seven miles down the Mississippi River from the heart of Minneapolis. Here the Minnesota River joins the larger Mississippi and here also, a mile nearer, stands historic old Fort Snelling, guarding the meeting point of the two ancient waterways.

Minnesota is the Land of Ten Thousand Lakes. Minneapolis, the larger of the Twin Cities, is a city of lakes and parks, homes and gardens. Within the city limits are ten lakes, six of them of large size. All are public property, having been acquired early by men of vision on the Park Board. About these lake parks are grouped some of the finest residence districts to be found anywhere. There are in all 131 public parks and playgrounds, the largest Glenwood Park, including 681 acres of groves, gardens of wild flowers, municipal golf links and bathing beaches. Here is a gigantic ski slide for winter sports. Skating, outdoor hockey and horse racing on the ice are amply provided for on Lake of the Isles. Commodious and comfortable enclosed hockey rinks provide the public with opportunity to witness this dashing sport.

The City of Minneapolis was chartered in 1854, and recently celebrated its 75 anniversary. Today the population exceeds 500,000, and one million people reside within a radius of 25 miles. Men of vision and power were its founders and to these, coup'ed with its strategic location, are due its tremendous growth and influence. The lumbering industry, once of prime importance, has to some extent given way to other industries which occupy the almost uncounted acres along the upper river that were once covered by the sawmills. The milling of flour, while still of enormous importance, is no longer the only outstanding activity, although the great names on sacks of Minneapolis flour may be found in nearly every metropolis and hamlet of the globe. The slogan, "Eventually, Why Not Now," may be said to express the spirit of the people.

as well as the invitation of the makers of the flour thus advertised. The leading industries include printing and publishing, general construction, and the manufacture of motor vehicles and parts; structural and ornamental iron; mill-work and other lumber products; heat regulators; foundry products; linseed oil; cake and meal; knit goods; bakery products; flour, breakfast foods and other food necessities.

The public school system is said to be one of the best in the country. The Minneapolis Public Library has twenty branches and fifteen stations. Illiteracy claims only 1.2 per cent of the population, a figure said by those who know to be the lowest among the larger cities of the United States.

In point of size, the University of Minnesota is among the first five in the country. In 1928-29 it registered 16,713 students. The same year the Medical School registered 751 graduates. The Graduate School of the University supervises all graduate work, including that for advanced degrees in medicine and its specialties, both on the main campus in Minneapolis and at the Mayo Foundation in Rochester, ninety miles away.

The main campus of the University lies in a great bend of the Mississippi, is in the south east section of the city, and can be reached in a few minutes from the principal hotels, as well as from the Auditorium, where the Scientific Assembly will be held. It covers twenty-four city blocks and the newer portion is in a pleasing style of architecture on a comprehensive plan by Cass Gilbert. Built in this newer style, the Medical School and University Hospitals occupy a commanding site with an inspiring view down the great gorge in which the river lies. To the Elliott and Todd Memorial Hospitals and the Cancer Institute have just been added the Eustis Hospital for Children, a new general pavilion with improved quarters for the Out-patient Department, and a new hospital and dispensary for the Students' Health Service. These additions will all be in operation by the time the College meets in February.

The laboratories of the State Department of Health are on the campus near the Medical School and provide added facilities for instruction in Public Health.

Beside the University Hospitals, twelve hospitals, most of them of major importance in the health and life of the city and its territory, are to be utilized in the Clinics of the session. Most important in this group is the Minneapolis General Hospital, with more than 600 beds, under a progressive and able Superintendent, a medical man whose work in this field has been notable.

Glen Lake Sanatorium, the Hennepin County institution for the tuberculous, located in a suburb of Minneapolis, but readily accessible from the Auditorium, has over 700 beds and is one of the largest and most modern institutions of its kind. Students from the University Medical School obtain instruction in tuberculosis, during stated periods of clerkship, under a permanent and visiting Staff whose work has attracted country-wide notice.

The campus of the Agricultural School is three miles from the main University Campus and lies within the city limits of St. Paul. Here may be found laboratories where outstanding work in chemistry, animal husbandry and horticulture is going on. Some of this work is of immediate interest to the physician and will be demonstrated during the scientific sessions.

Minneapolis is a center of culture for the Northwest. In the Art Institute have been gathered masterpieces of painting and sculpture, rare and notable tapestries and objects of art. There are larger collections in the great centers of the country, but the discrimination shown in selection and the taste used in display have called forth favorable comment from authoritative critics.

The Walker Art Gallery, provided and furnished by the late lumber baron, on a unique and centrally located site, gives an opportunity for viewing old masters. Miniatures, ancient jewelry and jades, as well as Greek, Egyptian and Chinese pottery, comprise a collection of peculiar character and interest.

The Minneapolis Symphony Orchestra has carried the name of the city to music lovers from coast to coast, through its annual tour. Great schools of music and the

arts have their homes in the commonwealth. The theatres are adequate and provide a variety of entertainment agreeable to every taste.

From the the wealth of material presented for study by this stately and yet charming city of the Northwest, soon to be our host, it has been possible to select only a few features for comment. The Municipal Auditorium might be described in extensive detail, for it has already proved to be the most suitable and attractive of meeting places for a session such as the one to be held during the week of February tenth. Whole blocks of buildings have been razed to provide a proper view and approach. The location is convenient to the hotels. When the Auditorium is to be used for one great meeting place, more than 15,000 people can be seated, and from any point vision and hearing are perfect. For the Scientific Assembly of the College, a suitable space at the stage end of the great structure will be walled off by immense, sound-proof curtains. Thus a comfortable hall is provided, with adequate seating facilities and protection from disturbing noises. Every device for the illustration of papers and the demonstration of specimens will be furnished. Before entering the hall of meeting, the visitor finds himself in a spacious and commodious lobby, where registration goes on with dispatch and ease, where all the exhibits will be suitably housed, and where the amenities may be practised at all hours when the attractions of the session are not too impelling.

The Auditorium will not, this time, be the center for making appointments for golf, fishing or canoe trips. Note carefully the date, which was specifically requested by the Fellows from the South. The Auditorium, the hotels and the homes, as well as the cars and taxicabs of Minneapolis, however, boast of a more comfortable temperature in February than one has ever been able to find in that same month in Southern California. Come to Minneapolis in February and find a wealth of scientific lore in the sessions, a plethora of interesting Clinics and demonstrations in the hospitals and laboratories, and a warmth of wecome from your friends of the medical profession. If you have no friends there now, you will be sure to make them when you come. Bring your overcoat, or if you have none, come anyway and borrow one, for the wealth of this metropolis of the Northwest is so great that every citizen of Minneapolis has at least two.

A postgraduate course for the benefit of general practitioners was inaugurated last September by the Medical Staff of St. Michael's Hospital, Toronto. The Fellows of the College who addressed the meetings and conducted clinics were: Drs. J. H. Elliott, J. D. Loudon, H. McPhedran, A. J. McKenzie, E. A. Broughton and F. C. Harrison.

Dr. Lewellys F. Barker (Fellow), Baltimore, is the first occupant of the newly established visiting professorship in the Medical School of the University of California. Dr. Barker will deliver a series of lectures and conduct clinics at the California institution during March, 1930.

Dr. James S. McLester (Fellow), Birmingham, Ala., and Dr. Charles C. Bass (Fellow), New Orleans, will deliver addresses before the Issaquena-Sharkey-Warren Counties (Miss.) Medical Society at its December meeting.

Dr. Ralph Pemberton (Fellow), Philadelphia, and Dr. Logan Clendening (Fellow), Kansas City, were speakers at the Kansas City Annual Clinical Conference, October 7-11.

Dr. Clyde L. Cummer (Fellow), Cleveland, was a member of the committee on arrangements for the annual meeting of the Fifth District (Ohio) Medical Society at Cleveland on September 20. The meeting was devoted to a discussion of the diagnosis and treatment of cancer. Dr. Joseph McFarland (Fellow), professor of pathology at the University of Pennsylvania School of Medicine, was one of the guest speakers.

Dr. George T. Harding, Jr. (Fellow), Columbus, addressed the Pickaway County (Orio) Medical Society at Circleville, August 2, on "Hobbies and Specialties" in the practice of medicine.

Dr. Henry L. Bockus (Fellow), Philadelphia, delivered two addresses before the joint meeting of the Jackson County (Mo.) Medical Society and the Kansas City Southwest Clinical Society, September 10. His subjects were: "Syphilis Associated with Pathology in the Upper-Gastro-Intestinal Tract" and "Duodenal Stasis".

Dr. Ray M. Balyeat (Fellow), Oklahoma City, is President of the American Society for the Study of Allergy.

Dr. E. C. Thrash (Fellow), Atlanta, gave a report of the Portland session of the American Medical Association before the Fulton County (Ga.) Medical Society on August 1.

At the twenty-sixth annual meeting of the Nevada State Medical Association, low), Rochester, Minn., and Dr. Albert Sept. 27-28, Dr. Howard R. Hartman (Fel-Soiland (Fellow), Los Angeles, Calif., spoke on "Medical Treatment of Ulcer of the Stomach and Duodenum" and "Carcinoma of the Breast", respectively.

Dr. James Allen Jackson (Fellow), Danville, Pa., addressed the Montgomery County (Pa.) Medical Society at Norristown, September 4, on mental hygiene.

Dr. Stuart Graves (Fellow), University, Ala., has been appointed acting health officer of Alabama by the State Board of Health, during the absence of Dr. Douglas L. Cannon, who has been ill for some time.

Dr. Edwin Schisler (Fellow), St. Louis, Mo., addressed the San Diego County (Calif.) Medical Society on heart disease, September 10.

Among speakers at the 109th annual meeting of the Michigan State Medical Society at Jackson, September 17-19, were the following Fellows of the College: Dr. William Gerry Morgan, Washington, D. C.; Dr. William Englebach, St. Louis, Mo.; Dr. Frederick A. Willius, Rochester, Minn.; Dr. George E. Brown, Rochester, Minn.; Dr. Frederic W. Schultz, Minneapolis, Minn.

Dr. Arthur C. Morgan (Fellow), Philadelphia, and Dr. Edgar M. Green (Fellow), Easton, were speakers at the opening of the newly reconstructed Portland (Pa.) Hospital.

Dr. Colonel B. Burr (Fellow), Flint, Mich., addressed the Oakland County (Mich.) Medical Society, September 12, on "Professional Contacts and Near-Contacts".

Dr. Hugh S. Cumming (Fellow), Surgeon General of the U. S. Public Health Service, delivered an address before the sixtieth annual meeting of the Medical Society of Virginia at the University of Virginia, Charlottesville, October 22-24.

Dr. Horton R. Casparis (Fellow), Nashville, Tenn., addressed the Central Tri-State Medical Society at Huntington, W. Va., Sept. 19, on "Treatment of Tuberculosis in Children".

Dr. James D. Bruce (Fellow), Ann Arbor, Mich., as councillor, with officers of Livingston, Lenawee, Monroe and Washtenaw (Mich.) County Medical Societies, conducted a meeting of members of those societies at the state sanatorium at Howell, October 8. Dr. Stuart Pritchard (Fellow), Battle Creek, conducted one of the clinics.

Dr. Guy L. Kiefer (Fellow) Lansing, Mich., is the State Commissioner of Health.

Dr. James M. Hutcheson (Fellow and Governor for Virginia), recently addressed the Northampton County (Va.) Medical Society at Nassawadox, Va., on "Heart Pains".

Dr. William A. Evans (Fellow), Detroit, and Dr. James H. Hutton (Associate), Chicago, were speakers at the 52d annual meeting and dinner of the Chicago Gynecological Society on October 11.

Dr. James Alex. Miller (Fellow), New York City, was recently elected chairman of the Committee on Public Health Relations of the New York Academy of Medicine.

Dr. James E. Paullin (Fellow), Atlanta, Dr. Warfield T. Longcope (Fellow), Baltimore, and Dr. Walter L. Bierring (Fellow), Des Moines, are among the trustees of the Frank Billings Lectureship Fund, established during the Minneapols meeting of the American Medical Association by the Section on Practice of Medicine. The object of the fund is to provide a lecturer each year before the Section. Dr. Bierring will be the Treasurer.

At the regular meeting of the North Pacific Society of Internal Medicine, on September 14, at Tacoma, Wash., Dr. Charles E. Sears (Fellow), Portland, Ore., was elected President and Dr. Lester J. Palmer (Fellow), Seattle, Wash., was re-elected Secretary-Treasurer. This Society was organized about three years ago and its membership is limited to forty physicians, whose practices have been restricted to the field of internal medicine for a period of at least five years. Several of its members have been elected to Fellowship in the American College of Physicians.

The following Fellows of the College were on the program of the sixty-sixth session of the Homeopathic Medical Society of the state of Pennsylvania held at Philadelphia, on September 24, 25, and 26. Dr. Ralph Bernstein, Dr. Carl V. Vischer, Dr. E. Roland Snader, Jr., Dr. G. Harlan Wells, Dr. G. Morris Golden. Dr. G. Harlan Wells of Philadelphia was chairman of the section on Clinical Medicine.

Dr. H. D. Lawhead (Associate), Woodland, Calif., has retired from active practice.

Dr. William R. Dancy (Fellow), Savannah, Ga., is President of the Medical Society of Georgia. Dr. Dancy was recently appointed a member of the Board of Judges (Georgia State Committee), by the American Chemical Society, to pass upon essays rendered upon this Society in competition for the prizes which it offers.

Dr. Herman M. Baker (Fellow), Evansville, Ind., has been highly commended for the successful arrangements made for the Indiana State Medical Association meeting at Evansville, September 25, 26, and 27. Dr. R. H. Beeson (Fellow), Muncie, Ind., was chairman of the Medical Section and introduced the following Fellows of the College, who gave addresses: Dr. Elliott P. Joslin, Boston, Mass., "The Abolition of Diabetic Coma in the United States"; Dr. Francis Eugene Senear, Chicago, Ill., "Cutaneous Tuberculosis and General Medicine"; Dr. Robert M. Moore, Indianapolis, Ind., "Subacute Bacterial Endocarditis—Some Clinical Observations"; Dr. Walter Clement Alvarez, Rochester, Minn., "What Shall We do for the Patient With Nervous Indigestion?"; Dr. Ralph Pemberton, Philadelphia, Pa., "Arthritis". Dr. Moore's paper was discussed by Dr. Edgar F. Kiser (Associate), Indianapolis. Dr. Moore was elected chairman of the Medical Section for 1930.

Dr. R. H. Beeson is President of the Muncie Academy of Medicine. At the meeting of the Academy, on October 2, Dr. Larue D. Carter (Fellow), of Indianapolis, delivered an address on "Chronic Encephalitis".

Lt. Col. W. S. Shields (Fellow), heretofore stationed at the Fitzsimmons Hospital, Denver, Colo., was recently transferred to Ft. Sam Houston, Texas, to relieve Col. Roger Brooke (Fellow), as chief of the medical service.

Dr. E. Roland Snader, Jr. (Fellow), Philadelphia, was elected Secretary for the fifth consecutive year of the Homeopathic Medical Society of the State of Pennsyl-

vania at its recent meeting. Dr. Snader is the author of an article, "A Modern Conception of Treatment of Cardio-Vascular Syphilis", in the September issue of the Hahnemannian Monthly.

The Coney Island Hospital of Brooklyn, N. Y., has recently undergone a reorganization under the direction of Dr. William Schroeder, Jr., Commissioner of Hospitals. of the teaching units of the Long Island It is reported that this Hospital will be one College Hospital. Dr. Philiip I. Nash (Fellow), has been appointed Chief of Medicine; Dr. Thomas J. Longo (Fellow), Attending in Medicine; Dr. Judson P. Pendleton (Fellow), Chief of Pediatrics; Dr. Nation T. Beers (Fellow), and Dr. J. M. VanCott (Fellow), members of the Consulting Staff.

Dr. E. Sanborn Smith (Associate), of Mo., and lecturer on Pediatrics in the Kirks-Grim-Smith Hospital and Clinic, Karksville, ville State Teachers College, has been placed on the State Board of Health by Governor Caulfield.

Dr. Carl V. Vischer (Fellow), Philadelphia, is the author of a case report, "Chronic Ulcerative Colitis-Perforation and Peritonitis," which was published in the September number of the Hahnemannian Monthly.

Dr. John A. Lichty (Fellow and Regent), at a recent meeting of the Seventh District Medical Society, held at the Clifton Springs Sanitarium & Clinic, Clifton Springs, N. Y., was re-elected Secretary of the Society for the ensuing two years. Papers were read at the meeting by Dr. L. G. Rowntree (Fellow) of the Mayo Clinic, Dr. Edward Archibald of McGill University, Dr. Louis Hamman of Johns Hopkins University, and Dr. Frank A. Kelly of Detroit.

Dr. C. Harvey Jewett (Fellow), of the Clifton Springs Sanitarium & Clinic, on October 8, as President of the Ontario County Medical Society, presided at a dinner in celebration of his father's, Dr. John H. Jewett, fiftieth anniversary in practice in this County. Dr. Jewett's grandfather and gretat uncle, doctors of the same name, have furnished a continued service of 110 years in the practice of medicine in this County. The address of the evening was given by Dr. J. H. VanderVeer, President of the State Medical Society of New York.

Dr. Joseph McFarland (Fellow), Professor of Pathology at the University of Pennsylvania School of Medicine, is the author of an aorticle, "Heredity in Malignant Disease," in the October number of the Pennsylvania Medical Journal.

Dr. Herman B. Allyn (Fellow) has resigned as Visiting Physician to the Philadelphia General Hospital, also as President of the Medical Board, and has accepted an appointment as Consulting Physician.

Dr. Noel F. Shambaugh (Fellow) recently resigned as assistant professor at the University of Michigan to accept an appointment on the medical faculty of the University of Southern California. Dr. Shambaugh is now residing in Long Beach, Calif.

Dr. P. P. McCain (Fellow), Sanatorium, N. C., was elected President of the Southern Tuberculosis Association at its annual meeting in Nashville, Tenn., Sept. 25, 26 and 27. Dr. McCain served last year as President of the Southern Sanatorium Association.

Dr. Myer Solis-Cohen (Associate), Philadelphia, Pa., read a paper on "Tuberculin in Diagnosis and Treatment in Infancy and Childhood, With a Method for Determining the Appropriate Therapeutic Dose in the Individual Case" before the Section on Pediatrics of the Medical Society of Pennsylvania, at Erie, on October 1.

Dr. Solis-Cohen also read a paper, with Dr. Rachel Ash, on "The Action of Whole Fresh Blood upon Pneumococci" before the Pathological Society of Philadelphia on October 10.

Under the Secretaryship of Dr. Harold Swanberg (Fellow), Quincy, Ill., the Adams County Medical Society of Illinois held its annual fall clinical conference at Quincy, October 14. The program was known as the "All-Philadelphia Program," since every speaker was selected from the faculties of the School of Medicine and of the Graduate School of Medicine of the University of Pennsylvania.

Dr. Leroy H. Sloan (Fellow), Chicago, addressed the Winnebago County Medical Society, Rockford, Ill., October 8, on "Fundamental Principles in Neurologic Diagnosis.

Dr. Louis A. M. Krause (Fellow) Baltimore, Md., at the opening of the fall semester of the University of Maryland School of Medicine, was promoted to Assistant Professor of Medicine.

Dr. Anton J. Carlson (Fellow) and Dr. Arno B. Luckhart of the University of Chicago have produced a film showing the movements of the alimentary tract in experimental animals. This film was presented before the Omaha-Douglas (Nebraska) Medical Society on September 24.

Dr. Nelson G. Russell (Fellow), Buffalo, N. Y., has been appointed to the chair of professor of medicine in the University of Buffalo School of Medicine.

At the recent annual meeting of the Medical Society of the State of Pennsylvania at Erie, Dr. William T. Sharpless, West Chester, Pa., was elected President; Dr. Ross V. Patterson (Fellow), dean of Jefferson Medical College, Philadelphia, was made president-elect; and Dr. Alexander H. Stewart (Fellow), Indiana, Pa., was elected one of the vice presidents.

Dr. Roy R. Snowden (Fellow), Pittsburgh, Pa., addressed the Mahoning County Medical Society, Youngstown, Ohio, September 17, on nephritis.

Dr. Arthur C. Morgan (Fellow), Philadelphia, Pa., addressed the Summit County (Ohio) Medical Society, Akron, October 8, on "The Treatment of Acute Cardiac Tragedies."

Dr. Abraham H. Aaron (Fellow), Buffalo, N. Y., addressed the Eighth District (Ohio) Medical Society, October 3, on Gastro-Intestinal Therapeutics."

OBITUARY

Dr. Rudolph William Gelbach (Fellow), Hoboken, N. J., died at his summer home, Keene Valley, N. Y., August 2, 1929, of recurrent carcinoma of the kidney; aged 72.

Dr. Gelbach was born in Pfalz, Germany, November 30, 1857, was educated in the Universities of Strassburg, Munich and Würzburg, filled the compulsory term of military service by work in military hospitals, and received his medical degree from the University of Munich in 1881. He came to America in 1883, and for two years practiced in Mendota, Illinois. Coming to Hoboken, New Jersey, in 1886 to visit his parents, he was induced to help an older physician who was ill, and he was soon so busy that he abandoned his plan to return to Illinois and remained in Hoboken for the rest of his active life.

For many years, Dr. Gelbach was visiting surgeon at St. Mary's Hospital, Hoboken, visiting physician at Christ Hospital, Jersey City, and consulting physician at North Hudson Hospital, Weehawken, and at the Farr Sanatorium, Hoboken. He was known throughout Hudson County for his skill in diagnosis, and is said to have kept himself thoroughly conversant with all new methods of diagnosis and

treatment. He was always ready to assist other physicians in emergencies without thought of remuneration; his ready, spontaneous wit and humor made him a most agreeable associate.

During the last three years of his life, he gave up private practice and confined his work entirely to consultations. In October, 1927, he underwent nephrectomy, made a good recovery and was comfortable for over one year when recurrence in abdominal glands caused his death on August 2 of this year.

Dr. Gelbach's chief diversion was hunting; he had a wonderful collection of animal heads to show for his trips. He hunted and brought game from the Rocky Mountains, Labrador, New Brunswick, Lower California, Mexico and Africa. In October, 1928, in spite of his depleted physical condition, he travelled alone in Spain, Italy, Sicily, Tunis and Egypt.

Surviving Dr. Gelbach are two sons, one daughter, one brother and three sisters.

He was a member of the New Jersey State Medical Association, the Hudson County Medical Society, the American Medical Association, the New York Academy of Medicine, and had been a Fellow of the American College of Physicians since 1920.

Circulation
of
ANNALS OF INTERNAL MEDICINE
October, 1929

United States	2,135
Canada	56
Panama and the Canal Zone	8
Hawaii	4
Germany	3
Mexico	3
Porto Rico	3
Australia, Cuba, India and Philippine Islands (2 each)	8
Argentine, Belgium, Central America, China, Denmark, England, France, Haiti, Italy, Japan, Java, Roumania, Russia, South Africa and Switzerland (1 each)	15
	2,235

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Connecticut	27	Ohio	120
Delaware	2	Oklahoma	26
Dist. of Columbia	93	Oregon	19
Florida	15	Pennsylvania	223
Georgia	55	Rhode Island	7
Idaho	3	South Carolina	7
Illinois	110	South Dakota	1
Indiana	51	Tennessee	33
Iowa	24	Texas	71
Kansas	13	Utah	3
Kentucky	37	Vermont	2
Louisiana	42	Virginia	26
Maine	17	Washington	24
Maryland	45	West Virginia	30
Massachusetts	59	Wisconsin	47
Michigan	135	Wyoming	1
Minnesota	68		
Mississippi	10		2,135
Missouri	62		
Montana	7		
Nebraska	36		
New Hampshire	4		

October 16, 1929. Certified Correct:

E. R. LOVELAND,
Executive Secretary.